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## RADIO-ISOTOPES: THEIR PRODUCTION AND USES.[1]

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To understand the production and application of radio-isotopes, it is necessary to know something of the modern theory of the structure of the atom.

As early as 500 B.C. Greek philosophers postulated that if matter was successively divided into smaller and smaller fragments, there would finally remain particles which could no longer be divided, and these—from the Greek word for indivisible—were called atoms. This hypothesis was used by Dalton in 1800 to explain the observed facts of chemical combination. He assumed that the atoms of one element were all similar, but that the atoms of different elements differed from one another. If two elements combined together to form a chemical compound, then this was really the union of atoms of the two elements; for example, a molecule of water was formed by two atoms of hydrogen and one of oxygen. The atomic theory served the chemists to explain experimental results very well for almost a century, and the idea of an atom which was indivisible became firmly established.

The last five years of the last century were remarkably fruitful for physical research. In 1895 Röntgen discovered X rays, and one of the important properties of these rays was found to be the power of ionizing gases—that is, of making gases (which were normally good insulators) electrically conducting. One of the foremost investigators of the conduction of electricity was J. J. Thomson. Thomson ionized gases at low pressure by means of X rays. By subjecting the ions to an electric field, he caused those charged positively to move in one direction, and those charged negatively in the opposite direction. By using hollow electrodes, Thomson was able at will to separate either the positive or negative ions into a separate enclosure and there investigate their properties. By 1897 he had shown that the electrical charges on the positive and negative ions were equal in magnitude, that the mass of the positive ion of any gaseous element was approximately the mass of the atom of that element, and that no matter what gas was used, the negative ion had always the same mass. The mass of the negative ion was very small compared with that of the positive ion. Thomson had therefore split the "indivisible" atom and had shown that the atom was divided into two parts, the negative part of which was common to all atoms, and this he called the electron.

The discovery of radio-activity by Becquerel in 1896 had been followed the next year by the isolation of radium by the Curies. Experiments soon showed that radium (and its products) emitted a penetrating corpuscular radiation, called $\beta$ rays, and that these $\beta$ rays were actually electrons, thus confirming Thomson's conclusion that the electron was an essential constituent of an atom. Further confirmation of the theory of atomic constituents resulted from the discovery that radium gave off, in the form of $\alpha$ rays, ionized atoms of helium, which took up electrons to form normal helium atoms.

Thomson then put forward a theory of atomic structure. Since an atom was electrically neutral, it should consist of equal numbers of positively and negatively charged ions. The negative ion was the electron. Thomson postulated a positive elementary particle, the proton. Since the major portion of the mass of the atom was concentrated in the positive ion, the proton was considered to be much heavier than the electron, and therefore presumably of a greater volume. Thomson's atom was therefore pictured as a positive sphere of electricity made up of protons, in which the electrons were dispersed like plums in a pudding. The lightest element, hydrogen, with a mass of one, had one

[1] Read at a meeting of the Victorian Branch of the British Medical Association on April 7, 1948.

proton and one electron; the next element, helium, with a mass of four, had four protons and four electrons; and so on with the heavier elements.

This theory of the structure of the atom was, however, soon found to conflict with experimental results. Rutherford investigated the manner in which α rays (positively charged particles emitted by radioactive atoms) were deflected by thin foils of light materials. By measuring the angles at which the α rays were deflected, he was able to show that the α rays actually went closer to the centre of the atom than the radius—that is, the positively charged particle actually penetrated within the sphere of positive electricity. On the basis of the forces of repulsion between the positive charges, however, this penetration could not take place. Consequently, Rutherford and Bohr in 1913, aided by experimental data obtained in the study of optical and X-ray spectra, put forward a second theory of the structure of the atom. Here the mass of the atom was concentrated in a nucleus at the centre of the atom, while the electrons moved in orbits around the nucleus in much the same way as the planets move around the sun. The number of orbital electrons was equal to the atomic number of the element (that is the position of the element in the periodic table), and the nucleus was composed of a number of protons equal to the number of electrons, together with a sufficient number of pairs of electrons and protons to make up the mass of the atom. The orbital electrons were arranged in series to account for the general chemical properties of the atoms.

The concept of atoms being composed of protons and electrons would appear to cause the atomic mass of any element to be an integral number of times that of the elementary atom, hydrogen. In fact, however, although some elements did have essentially integral atomic masses, others differed very definitely from an integral value; for example, the atomic mass of chlorine was 35·5. To overcome this difficulty, Soddy suggested that an element might exist in more than one form, the number of orbital electrons being the same in all forms, but the mass of the nucleus being different. These forms, representing atoms with the same chemical properties, but with different atomic masses, were termed isotopes. The existence of isotopes was soon shown experimentally by Aston, who showed, for example, that chlorine could exist in two isotopic forms, with masses of 35 and 37, and that the proportion of the two forms was such that the mean mass was 35·5.

In 1919, Rutherford, in further investigations of the passage of α rays through gases, showed that the old dream of the alchemists of transmuting elements really could come true, in that the nucleus of one element could be altered to form another element. In the same way as chemical equations can be represented by atomic equations, it was found possible to write nuclear equations to represent these transmutations as follows:

$$_2He^4 + _7N^{14} = _8O^{17} + _1H^1$$

Rutherford found that the α particles, in passing through nitrogen, occasionally struck a nitrogen nucleus, and as a result of a rearrangement of the nuclear components oxygen and hydrogen were formed.

Here the α particle is represented by the helium nucleus, the superscript four representing the atomic mass, and the subscript two representing the atomic number of helium. It will be seen that there is equality of the totals of the superscripts (and of the subscripts) on each side of the equation.

In this transmutation, Rutherford was using the α particle, travelling with its natural velocity of ejection, as an atomic projectile. The energy of this projectile was, however, too small to cause more than a few types of transmutation, and physicists everywhere sought for more powerful atomic projectiles. Amongst these Cockcroft and Walton, by accelerating protons (nuclei of hydrogen) by a potential difference of hundreds of thousands of volts, found in 1932 another transmutation of a remarkable type. When the protons were directed onto lithium atoms, the nuclei were rearranged to form two atoms of helium, and a considerable amount of energy was liberated. The nuclear equation could be written thus:

$$_1H^1 + _3Li^7 = _2He^4 + _2He^4$$

In seeking to find the source of the released energy, Cockcroft and Walton substituted the accurately known atomic masses, to find that a total mass on the left-hand side of 1·0081 + 7·0170 = 8·0251 did not equal that on the right-hand side of 4·0034 + 4·0034 = 8·0068, but that a loss of 0·0183 mass unit had occurred. The released energy could be explained if the law of conservation of energy, and not the law of conservation of mass, was vital. Here atoms had been smashed, and some mass had been destroyed, and an equivalent quantity of energy released.

Two further important discoveries occurred about this time. In 1932, Chadwick, in observing the passage of α particles through beryllium, detected a very penetrating corpuscular radiation which was soon shown to have approximately the mass of the proton, and to be uncharged; to this particle was given the name neutron. The neutron, because of its large energy, must have originated in the nucleus of the atom, and it was suggested that the neutron was really a proton and an electron in close association. On this basis, the original Rutherford-Bohr conception of the nucleus as comprising a number of protons to equal the atomic charge, and a number of pairs of protons and electrons to make up the atomic mass, became a number of protons *plus* a number of neutrons. The neutron, an uncharged particle with reasonable mass and high energy, could easily penetrate the nuclei of atoms, and provided a new and powerful atomic projectile.

In 1934, Irene Curie and her husband Joliot, in investigating the passage of α particles through aluminium, discovered a residual radiation which persisted after the exciting source of α rays had been removed, and which decreased according to the natural laws of radioactive decay.

In another experiment, in which α particles were caused to strike boron, it was found that a neutron was emitted, an unstable isotope of nitrogen was formed, and subsequently this nitrogen atom, disintegrated according to the normal laws of radioactive decay, emitted a $\beta$ ray and became a stable atom of carbon.

The discovery of the naturally radioactive elements in 1897 by Marie Curie and her husband had been followed in 1934 by the discovery of artificially radioactive elements by the daughter Irene Curie and her husband.

The discovery of the neutron on the one hand, and of artificial radioactivity on the other, stimulated physicists to almost frenzied attacks upon the nucleus. Bigger and better atom smashing machines were devised. The nucleus of hydrogen ($H^1$) (the proton) and that of its isotope deuterium or heavy hydrogen ($H^2$) (the deuteron) were accelerated in electric fields produced by voltages reaching one million. Hydrogen nuclei were successively accelerated in the cyclotron to impinge on targets of beryllium and produce neutrons. Within three years more than a hundred radio-isotopes had been produced and much had been learned concerning nuclear reactions.

Early in 1939 Hahn showed that when neutrons impinged upon one of the natural isotopes of uranium, the uranium nucleus disintegrated into nearly equal fragments, and considerable amounts of energy and more neutrons were released. These neutrons could then under certain circumstances cause further uranium atoms to disintegrate so that a spontaneous or chain reaction could be set up. The war came, and with it renewed activity in research into the release of nuclear energy culminating in the production of the atomic bomb.

The results of war-time activities in nuclear energy are now being made available for peaceful purposes. It has been possible, in the uranium pile, to control the rate of disintegration of the uranium, so that copious quantities of neutrons are available and these can be used to produce radio-isotopes in tremendous quantities. There are now more than three hundred known radio-isotopes, many elements existing in more than one form.

For example, there are four known isotopes of phosphorus, with atom masses of 29, 30, 31 and 32 respectively.

Of these, $P^{31}$ is the naturally occurring stable isotope. $P^{29}$ has a half-life[1] of less than ten seconds, $P^{30}$ of two and a half minutes, and $P^{32}$ of 14·3 days. Because of their excessively short lives, $P^{29}$ and $P^{30}$ are of limited value, and $P^{32}$ is the isotope most frequently used. Even the $P^{32}$ isotope can be produced in three different ways, by the bombardment of either the stable $P^{31}$ isotope, or of the $S^{32}$ stable isotope of sulphur, according to the following nuclear equations. The first two reactions are usually employed in the uranium pile, the last one in the cyclotron.

$$_{15}P^{31} + {}_0n^1 = {}_{15}P^{32} + \gamma \text{ ray}$$
$$_{16}S^{32} + {}_0n^1 = {}_{15}P^{32} + {}_1H^1$$
$$_{15}P^{31} + {}_1H^2 = {}_{15}P^{32} + {}_1H^1$$

In all cases $P^{32}$ decays in the following way to leave a stable isotope of sulphur:

$$_{15}P^{32} = {}_{16}S^{32} + \beta \text{ ray}$$

Radio-isotopes may be used in medicine in two ways. Since a radio-isotope of, for example, sulphur has the same chemical (and presumably physiological) properties as ordinary sulphur, it will be utilized in the same way by an organism. The passage of the isotope through the organism can, however, be traced by means of the radiation which is emitted. It will be remembered that the migratory habits of birds and fish have been studied by "tagging" or marking a certain number; the identification of these tagged individuals after capture at various stages in their life can be used to determine the habits of the species. Further, during the war, a small number of bullets which left a luminous trail in the air were introduced at intervals into the belts of machine-gun ammunition so that the gunner could detect the trajectory of the stream of projectiles by means of the "tracer" bullets. Because of the similarity of these processes of using a few marked samples to determine the behaviour of a group, radio-isotopes are often called "tagged" or "tracer" elements.

The radiation from the tracer element can be detected by means of a Geiger counter (which reacts to single ionizing particles), a sensitive ionization chamber, or a photographic plate. As little as one radioactive atom in ten or a hundred million of the natural isotope is sufficient for recognition. Tracer elements are therefore powerful tools in investigating metabolic processes, and permit observations of the actual transfer of an element from one cell constituent to another. Already much has been learned regarding physiological processes, and much more can be expected.

The tracer method of study is proving a valuable complement to histological examination. Alternate microtome sections of thyreoid tissue can be selected from a patient to whom radio-iodine has been administered; one of these can be stained in the usual way, and the other can be placed on a fine-grained photographic plate and an autoradiograph obtained. When the section and the autograph are examined microscopically side by side, the actual location of the absorbed radio-isotope can be determined. Since there is evidence that elements are absorbed to different extents by healthy and diseased cells of the same type, there is promise that tracer elements can be used as an aid to the diagnosis of some diseases.

The selective absorption of certain elements in particular organs promises a means of concentrating elements in their radio-active form in the organ and thus irradiating diseased cells with a minimum of radiation of adjacent healthy tissues. Already reports have been published of the use of radio-phosphorus in the treatment of blood dyscrasias, and of radio-iodine in certain diseases of the thyreoid.

Radio-isotopes must be regarded as a dangerous drug, as is radium. Many radio-isotopes, either in their initial or final form, may be dangerous poisons. Radium is lethal to humans in an absorbed amount of a few microgrammes; plutonium is ten to one hundred times more active. The emitted radiations, too, may cause permanent damage to body structures. For these reasons, the use of radio-isotopes must still be regarded as in the experimental stage, and the United States Atomic Energy Commission has therefore laid down very stringent regulations regarding the methods of distribution of radio-isotopes. Since Australian supplies are drawn from the United States, these regulations must also be observed here. Issues of isotopes can be made for use only in certain cases, full experimental records must be kept, and reports must be submitted at regular intervals. In this way it is believed that the fullest information regarding the possibilities and limitations can be accumulated in the shortest possible time.

It is not necessary to apologize for a physicist's speaking to a medical audience on radio-isotopes. The administration of these physical agents requires the services of experienced physicists in the preparation of samples with the correct dosage, in the determination, by means of delicate physical equipment, of the quantities of radio-isotopes which have been absorbed by the patient, in the assay of selected fluids and tissues, and finally in the ensuring of methods of protecting both patient and hospital staff from over-exposure of radiation. It can be expected that the future developments of techniques of utilizing radio-isotopes will be made as the result of the coordinated efforts of groups of specialists who are trained and equipped to do their several parts.

[1] Radioactive elements decay according to an exponential law, and the half-life is the period for the element to decay to one-half of its activity. If an element has a half-life of one hour, there will be one-half of its activity remaining at the end of the first hour, and half of that (that is, one-quarter) at the end of the second hour, one-eighth at the end of the third hour and so on.

## SOME USES OF THE ARTIFICIAL RADIOACTIVE ELEMENTS FOR INVESTIGATION AND TREATMENT.[1]

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I RETURNED from a visit to the United States of America and Great Britain only a few weeks ago. My visit was a short one, as attendance at the fourth International Cancer Research Congress was the prime object of the journey. In a message to this congress, the President of the United States announced that supplies of the radioactive isotopes would henceforward be made available to other nations for medical and research purposes, and he expressed the hope that the release of the isotopes would be one step forward in attaining the ultimate goal of a cure for cancer. The isotopes give us one more weapon in the war, but, according to present indications, their use is more for palliative than for curative purposes.

It is not necessary for me to do more than recapitulate briefly a few facts about the nature of the isotopes.

An atom is composed of a central nucleus surrounded by rings of electrons. The core consists of protons, of mass approximately unity, which are positively charged, and neutrons, again of mass approximately unity, but these particles are uncharged. The number of negatively charged electrons in the outer rings balances the number of positively charged protons in the nucleus, and the number of protons present determines the atomic number.

The chemical properties of the atom depend upon the number of peripheral electrons present, and hence upon the number of nuclear protons. The remainder of the nuclear weight is made up by a number of neutrons, which therefore do not affect the electrically charged proton-electron system. Various atoms of the same element exhibiting the same chemical properties may be of different atomic weights because of a variable number of neutrons in the nucleus. These atomic variants are called isotopes and may be stable or unstable in character.

[1] Read at a meeting of the Victorian Branch of the British Medical Association on April 7, 1948.

For example, hydrogen may exist as an atom with one proton balanced by a peripheral electron, the normal hydrogen atom; or it may occur as the heavy isotope with a neutron added to the proton of the nucleus. It has the same chemical properties, and so there is a "heavy" water with atoms of hydrogen of atomic weight two. Similarly, lead is a mixture of stable isotopes of atomic weight 206, 207 and 208.[1]

But many other isotopes exhibit a condition of nuclear instability, and sooner or later tend to undergo nuclear disruption with emission of perhaps $\alpha$, $\beta$ and/or $\gamma$ rays. This entails a loss of energy and the atom assumes a more stable form at a lower energy level. But always a new atom is formed in the process. Unstable isotopes emitting radiation are known as the radioactive isotopes.

But these atoms are quite capable of normal chemical behaviour until the incident of disintegration, and so they may be formed into chemical compounds and introduced in suitable form into the living organism to undergo the processes of metabolism natural to the element or compound concerned.

The isotopes are prepared by bombarding the nuclei of atoms with subatomic particles, usually neutrons or deuterons. The particles are usually accelerated to high speed as considerable energy must be added to the receptor nucleus.

Only a very minute proportion of atoms bombarded are subjected to change into the new form—perhaps one atom in 10,000,000 to 1,000,000,000. The unstable isotopes subsequently disintegrate according to the laws of radioactive decay. Some with short half-life are relatively unstable atoms—for example, $Na^{24}$ has a half-life of fourteen hours, while $C^{14}$ loses only half its mass in about 5000 years. The unit of radioactivity for clinical purposes is the millicurie. One milligramme of radium undergoes 37,000,000 atomic disintegrations per second; this same number of disintegrations per second among the atoms of a given isotope constitutes one millicurie. So, depending on the short or long half-life, a small or large number of unstable atoms must be present. For this reason 20 millicuries of $Na^{24}$ are clinically equivalent to one millicurie of active phosphorus, because the total energy liberated during their active lives is approximately equal.

Although such a minute fraction of the atoms of a solution for clinical use are radioactive, it is nevertheless astounding how small a mass of radioactive isotope is equivalent to one millicurie of activity.

TABLE I.
(*After* Quimby.[2])

| Isotope. | Half-life. | Milligrammes per Millicurie.[1] |
|---|---|---|
| $_{11}Na^{24}$ | 14·8 hours. | 0·000,000,113 |
| $_{15}P^{32}$ | 14·3 days. | 0·000,003,52 |
| $_{53}I^{131}$ | 8·0 days. | 0·000,008,05 |
| $_{88}Ra^{226}$ | 1590 years. | 1·0 |

[1] One millicurie equals 37,000,000 disintegrations per second.

Sensitive physical apparatus is available which allows even one atomic disintegration to be detected, and to such is added an integrator which allows thousands of disintegrations per minute to be counted with accuracy. So it is possible to apply a detector over any localized portion of the body and to detect not only the presence of an isotope, but even to estimate the quantity of isotope present at that site.

### PREPARATION AND FORM OF ISOTOPES.

For medical uses the isotope is prepared usually as a salt, and administration by oral or intravenous routes is practical.

$I^{131}$ is manufactured from tellurium and comes in a solution of $NaHSO_3$ (sodium sulphite); a small percentage of tellurium is also present.

$Na^{24}$ may be prepared in the cyclotron or the pile, and is finally used as either an active sodium chloride or sodium carbonate. Less than 1 in 10,000,000,000 of the sodium atoms are unstable.

$P^{32}$ is available as $Na_2HPO_4$ or $NaH_2PO_4$. The acid salt is less likely to be adsorbed onto the glass wall of containers, and is therefore issued for use in this form.

### FATE AND METABOLISM OF THE ISOTOPES.

The isotope in the compound administered undergoes the usual cycle of metabolic changes of the element considered until the moment of radioactive decay. Excretion by any of the usual channels, and natural radioactive decay, are the factors which diminish the amounts of active substance present. The radiation effects produced are of various types. A general bodily irradiation may be given if no selective absorption occurs; for example, sodium passes readily into all tissue fluids, while potassium readily enters into all body cells. Various tissues may absorb particular compounds in proportion to their physiological needs. If the take-up by the cells of a particular system is greatly in excess of the general absorption, it is justified to speak of selective absorption, and by making radioactive one element in the compound absorbed, a correspondingly increased dose of radiation may be administered to the receptor tissue.

Phosphorus is required in relatively greater amounts by cells undergoing mitosis on account of the increased nucleic acid metabolism and is naturally absorbed into tissues undergoing normal multiplication, like the skin or blood formative tissues. It is absorbed in large amounts by the reticulo-endothelial system. Because of selective pick-up, iron may be used for hæmatopoietic studies, or calcium and iodine for bone and thyreoid investigations respectively.

Cells of the reticulo-endothelial system readily ingest certain colloids. It has been demonstrated that there is differential pick-up of colloids according to colloid size by the reticulo-endothelial cells of different sites. Chromium is an inert physiological metal and chromium phosphate is obtainable in preparations of various colloidal size. Activated phosphorus can be incorporated. It is reported that the spleen will take up 80% of administered particles of a given size and so a "radiation splenectomy" may become possible.[3]

If selective localization takes place, the radiation effects are proportional to the dose and the susceptibility of the tissue. In a general bodily radiation gonads or hæmatopoietic tissues may suffer according to their particular sensitivity.

If excretion is rapid a great proportion of the total dose may be received by the excretory organs; for example, about 50% of the iodine absorbed is excreted within twenty-four hours. The renal parenchyma, ureters and bladder may then receive considerable dosage unless large quantities of fluids are administered to hasten the passage of the active isotopes through the excretory system.

It is possible that even with substances like sodium or phosphorus minute fractions of the order of 1% or less may undergo peculiar concentration, perhaps producing effects of ultimate damage that may not be obvious for years as late effects, or until many generations have passed as remote genetic mutation effects.

### TRACER STUDIES WITH ISOTOPES.

Every known atom has been obtained in more than one isotopic form—some stable, some unstable isotopes. However, some atoms do not readily produce radioactive isotopes—for example, aluminium and oxygen.

Stable isotopes can readily be recognized by chemical or physical means, and therefore molecules may be "tagged" with these atoms. Similarly, the radioactive atoms can be traced and detected by Geiger-Müller counters. Thus a vast field has been opened in the physiological and pathological branches of every biological science, which will enable biochemical processes to be investigated minutely. Further, many atoms present several isotopes, and so it will be possible to carry out differential studies.

### Examples of Tracer Studies.

Differential protein metabolism studies by means of two radioactive carbon atoms have been carried out. Tagging of other elements in protein chains is being extensively done. Calcium has been found essential for the intercellular protein-binding substance of squamous epithelium.

Calcium metabolism is being extensively investigated, and the relationships of phosphorus and vitamin *D* are being determined. Bone deposition is being aided by studies with radioactive strontium. It has been shown that the turnover and replacement of the individual calcium atoms in bone are remarkably quick.

Progressive diminution of mineral content including zinc has been found on the onset of cutaneous neoplasia with an increase of phosphorus in the cells. $P^{32}$ studies have helped in the study of nucleic acid metabolism and its relation to mitosis. Studies of sugar metabolism have been made by means of $P^{32}$. Radioactive zinc has been used to show that diminished quantities of this element are found in leuchæmic cells. Zinc is increased in the macrocytes in pernicious anæmia by a factor of four, but after liver therapy the concentration falls to normal.

Other examples of isotope tracer investigation include hæmoglobin studies by means of one or two different iron isotopes. The parts played by the accessory factors copper, manganese and zinc are being studied.

### Blood Volume Studies.

Krypton is an inert gas not metabolized by the body. Its inhalation in a radioactive form has enabled blood volume studies to be performed. It has been demonstrated by studies with $C^{14}$ that carbon monoxide is oxidized in the liver, and therefore methods of blood volume determination depending upon its use are unreliable.

### Blood Volume Determination with $P^{32}$.

Take ten millilitres of blood, wash off the serum and suspend the red blood cells in normal saline solution. Add a known amount of $P^{32}$ and incubate the mixture for thirty minutes in a round bottle resting on its side on rotating rollers to provide continual agitation. At the end of half an hour the $P^{32}$ has diffused inside the cells and the saline solution is spun off and replaced with further (non-active) saline solution. The difference in phosphorus content between the removed saline solution, less decay, and the original amount equals the amount retained in corpuscles. The blood cells, now suspended in the added fresh saline solution, are injected back. Test samples are withdrawn at intervals of half an hour to one and two hours for phosphorus dilution studies for blood volume determination.[4]

### Blood Circulation Time.

Smith and Quimby,[5] using radioactive sodium, have developed a test which has been found useful for determining efficiency of circulation in the lower extremities. A test dose of 100 microcuries of $Na^{24}$ is injected intravenously into the forearm. Curves have been constructed showing the limits of normality for young normal individuals in which increasing numbers of counts read at the sole of the foot are plotted against time. The sodium passes into the blood stream, but soon enters also the intercellular fluids, and so a steady build-up occurs dependent on circulating efficiency. The build-up is increased in conditions of inflammation, it is diminished in Mönckeberg's degeneration, while normal or high counts in arteriosclerotic diabetes indicate inflammation or an established collateral circulation. In *thromboangiitis obliterans* a normal reading indicates established collateral circulation. In hypertension, low, slightly low or normal counts may be obtained. Thoraco-lumbar sympathectomy is indicated in the presence of a low curve, contraindicated in the presence of the other readings. These findings must be correlated with the known state of arteriosclerosis and with the presence or absence of pulsation in the *dorsalis pedis* or popliteal vessels. A normal or high count in the absence of inflammation indicates conservative surgical procedures, as the collateral circulation has obviously become established.

### Radioactive Iodine.

Radioactive iodine has allowed intensive study of its absorption and metabolism in conditions of health and disease (*vide infra*). Studies with tracer doses enable states of hypothyreoidism or hyperthyreoidism to be determined. In the examination of children this is useful, as basal metabolic rate tests are not practicable. Neoplasia is usually associated with diminished pick-up, but this is subject to alteration if normal thyreoid function is eliminated.

### Therapeutic Uses of the Isotopes.

Therapeutic uses of the isotopes depend on the selective absorption of the isotope by the pathological tissue in such amounts that the tissue receives damaging amounts of irradiation, while other normal tissue irradiated, particularly the hæmatopoietic tissue, receives doses which do not cause permanent injury.

Up to the present, radioactive phosphorus has been used on account of its selective absorption by cells of the reticulo-endothelial system, and because of its increased absorption by dividing cells due to their increased nucleic acid content. This latter fact causes increased irradiation to be received by the multiform tissues, particularly gonads and blood-forming tissues, and thus imposes great limitations on the usefulness of the radioactive isotopes. In the neoplastic diseases concentration sufficient to produce any useful effect cannot be attained. But in the reticuloses (and chronic leuchæmias) a use has been established for $P^{32}$ or $Na^{24}$. $P^{32}$ produces a soft $\beta$ ray only and therefore the radiation acts at its site of absorption, an important therapeutic criterion. The selective absorption of iodine by the thyreoid is the outstanding example of concentration of one element by a single organ, and investigational and therapeutic use of this concentration effect is possible.

In general, with the exception of polycythæmia, a particular disease is not a specific indication for the use of isotope therapy. The special indications for the use of isotopes must be respected. The radioactive isotopes do not replace other forms of radiation therapy. Risks to patient, staff and administrator must be fully considered. Proper facilities for dispensing, administration and decontamination must be available before the use of isotopes is contemplated.

### Clinical Indications for $P^{32}$ or $Na^{24}$.

#### *Polycythæmia Vera.*

Isotopic control of *polycythæmia vera* has been more effective than any known form of therapy, producing longer remissions and absence of immediate or late ill effects, though it is not yet known whether the remote incidence of leuchæmia may not be increased. Isotope therapy therefore appears specifically indicated in true polycythæmia. Treatment must in all cases be controlled by regular blood studies.

In visits to clinics in the United States of America the following data were made available to me by the clinicians named.

Reinhard and Moore, Saint Louis: give four millicuries of $P^{32}$ intravenously and repeat in three and six months as necessary.

Pendergrass and R. Chamberlain, Philadelphia: give two doses of five millicuries of $P^{32}$ intravenously, forty-eight hours apart.

E. Chamberlain, Philadelphia: give 0·5 or 1·0 millicurie orally in orange juice each two or four hours respectively. (Dispense in labelled test tubes with extra amounts added to make up for decay until administration time.) A total of six to ten millicuries is needed in the first course. The effect is not usually seen for six to ten weeks on account of the long life of the red blood cell. Further treatment is necessary usually after three months. Thence carry out blood counts each six weeks. Remissions of six months may be expected.

Rubenfeld and Rosewit, Veterans' Administration Hospital, New York: 80 to 100 millicuries of $Na^{24}$ given orally are needed to produce the same effect as four millicuries of $P^{32}$. Give three doses of 30 millicuries at intervals of

one or two weeks. One millicurie of $Na^{24}$ is equivalent to about 0·5r of total body irradiation.

*Acute Leuchæmia.*

In general, in acute leuchæmia no useful effect has been obtained either in palliating the disease or in prolonging life by the use of radioactive isotopes. Occasional remissions have been seen in acute lymphatic leuchæmia. This group of diseases remains essentially untreatable.

*Chronic Myeloid Leuchæmia.*

Research investigation of chronic myeloid leuchæmia, particularly in the United States of America, up till the present has relied on treating groups of patients solely with the treatment method under trial, irrespective of any special indications for other forms of treatment that may have appeared. The results to be expected have therefore been determined and indications for the uses of the isotopes are now known.

Isotope therapy will cause remissions of the disease with subsidence of symptoms, restoration of white counts towards normal, decrease of anæmia and restoration of a more normal blood picture. The remission is temporary and the disease runs a course very similar to that seen under ordinary X-ray therapy. The isotopes are not so effective as X-ray therapy in reducing massive myeloid deposits or infiltrations, whether in spleen, liver, kidneys, glands or other sites. X-ray therapy should therefore be used when these manifestations are present. However, the isotopes are more effective than X-ray therapy in producing remissions in late stages when marrow is showing lack of response, with rising white blood cell counts, increasing anæmia and diminishing red blood cell and platelet counts. The isotopes are less likely to cause irradiation sickness than is external treatment. Thus the chief indications for the use of isotopes are the onset of marrow failure or the presence of distressing irradiation sickness.

If isotope therapy is being used, local external irradiation should be given if conditions of massive organic enlargement or other leuchæmic deposits or infiltrations are obvious. These conditions are generally present initially, and without evidence of marrow failure indicate the use of standard methods of X-ray therapy.

$P^{32}$ may be administered intravenously, or orally with allowance for 75% absorption. $Na^{24}$ for this purpose is orally administered with allowance for 100% absorption, 20 or 25 millicuries of $Na^{24}$ being therapeutically equivalent to one millicurie of $P^{32}$. The best and longest remissions appear after reduction of white blood cell count to the order of 5000 per cubic millimetre. The following data were given to me by the clinicians named.

Reinhard and Moore: A total dose of eight to twelve millicuries of $P^{32}$ is required during a course. Give two millicuries initially intravenously. Repeat the dose in two days; afterwards give one millicurie twice a week for two more weeks or until the leucocyte count begins to fall.

Pendergrass and R. Chamberlain; Small repeated dosage should be given intravenously to simulate whole body irradiation. Two millicuries of $P^{32}$ are given initially; then one millicurie on the second and third days; 0·5 millicurie on the fourth, fifth and seventh days; then 0·25 millicurie every second day till a total of seven or eight millicuries has been administered or till the blood count is seen to be falling satisfactorily.

E. Chamberlain: Give isotope $P^{32}$ orally; usually a total of twelve millicuries, one millicurie every four hours for three days.

Quimby, Presbyterian Hospital, New York City: $Na^{24}$ is preferred to $P^{32}$ for the treatment of all the reticuloses, leuchæmias or responsive neoplasms. It appears to be quite as effective as $P^{32}$ in spite of the absence of any localization effect.

Rubenfeld and Rosewit: $Na^{24}$ in oral doses of thirty millicuries is used for patients not responding to X-ray therapy. One dose is given each week till ninety millicuries have been administered. A remission of one to three months' duration is produced. No irradiation sickness occurs. Doses of fifteen to twenty millicuries do not produce more than a transitory effect at the five to seven day stage.

*Chronic Lymphatic Leuchæmia.*

Chronic lymphatic leuchæmia is likely to be associated with widespread glandular enlargement and with diffuse organic infiltration. The disease is more chronic and the red marrow does not suffer so early as in the myeloid form. Treatment follows exactly similar principles; the glandular and visceral enlargements indicate external therapy, and later marrow failure may indicate the use of isotopes in dosage similar to that employed for myeloid leuchæmia.

*Monocytic Leuchæmia.*

Monocytic leuchæmia is generally less responsive than the other varieties. Treatment follows exactly similar lines.

*Hodgkin's Disease.*

The use of isotopes in Hodgkin's disease has proved disappointing, and but little recession of glands is obtained. External X-ray therapy remains the method of choice in reducing the lymphadenomatous deposits. Nitrogen mustards have been more useful than the isotopes, but gland recessions are very transient; these drugs are indicated in Hodgkin's disease upon evidence of marrow infiltration and failure.

Possibly work on colloidal chromium phosphate may alter the status of the isotopes in the reticuloses.

*Brill-Symond's Disease, the "Lymphomata" and Boeck's Sarcoid.*

X-ray therapy is the most useful form of irradiation treatment in Brill-Symond's disease, the lymphomata and Boeck's sarcoid; nitrogen mustards may give accessory aid. The isotopes are not very useful, but occasionally satisfactory results have been reported.[6]

*The Lymphosarcoma Group.*

Treatment of the lymphosarcoma group with isotopes is again disappointing and not so satisfactory as external irradiation. Recession of gland masses may be dramatic, but is usually of very transient duration. Whole body irradiation does tend to cause irradiation sickness, and in the presence of diffuse deposits radioactive isotopes may be used, but in such cases more satisfactory results are likely to be obtained with the mustards.

The following dosages have been suggested to me:

E. Chamberlain: Isotope dosage follows that laid down for the chronic leuchæmias, but is pushed to limits of a severe leucopenia; eight to twelve millicuries of $P^{32}$ intravenously or ten to fifteen millicuries of $P^{32}$ orally seem to be the doses indicated; forty millicuries given orally is a dose outside the limit of safety.

Reinhard and Moore, St. Louis: An average amount of 7·0 millicuries of $P^{32}$ has been administered, the largest amount being 15·0 millicuries.

*Diffuse Neoplasms.*

The isotopes have been tried in cases of diffuse sarcomatosis and carcinomatosis without really useful effect.

*Carcinoma of the Head and Neck.*

Carcinomata of the head and neck, particularly anaplastic carcinoma of the naso-pharynx or oro-pharynx and secondary deposits in glands, have been treated without any real benefit.

*Diffuse Melanomatosis.*

No useful effect has been seen from the use of isotopes in diffuse melanomatosis. The mustards are worth trying.

*Diffuse Carcinoma of the Breast.*

No remission of primary glandular, visceral or cutaneous manifestations of carcinoma of the breast has been produced with either mustards or isotopes.

*Multiple Myelomatosis.*

The isotopes are useless in multiple myelomatosis, and chemotherapy has proved disappointing.

*Diffuse Neuroblastoma.*

No beneficial result is to be expected in diffuse neuroblastoma. One case of diffuse neuroblastoma was investigated at New York Presbyterian Hospital, by courtesy of Dr. Jacox, in which 200 millicuries of $Na^{24}$ had been administered over a period of six months. The patient had no significant recession of tumours, but the advance seemed to have been delayed. However, gross stomatitis and severe leucopenia were present. The stomatitis may have been a direct irradiation effect or a result of the agranulocytosis.

The dosages suggested to me are as follows:

E. Chamberlain, Philadelphia: Dosage in the groups named above follows the principles laid down for chronic myeloid leuchæmia, but dosage must be pushed to a stage of leucopenia. Oral courses of fifteen to thirty millicuries of $P^{32}$ are needed; a total of forty millicuries is the outer safe limit, one patient having died of this amount.

## The Uses of Radioactive Iodine.

The selective absorption of iodine by the thyreoid has been used both for tests of thyreoid function and for therapeutic purposes in simple and malignant diseases of the gland.

In the examination of children basal metabolic rate tests are impracticable, and tracer studies by means of $I^{131}$ have been found useful.[7] The uptake of the iodine is a measure of thyreoid function. An uptake of 10% or less at forty-eight hours indicates hypothyreoid states including cretinism; one of 10% to 15% is within normal limits, whereas values over 40% indicate hyperthyreoid states.

The tracer dose for an adult is sixty microcuries of $I^{131}$; for children a proportionately smaller dose (about six microcuries per stone) is used, according to weight.

TABLE II.

*Percentage Uptake in Thyreoids of Children at Forty-eight Hours after Test Dose of $I^{131}$.*

(*After* Quimby.)

| Age. (Years.) | Normal. | Abnormal. | |
|---|---|---|---|
| <1 | 12±4% | Cretinism | <1% |
| 1 to 4 | 10±3% | Myxœdema | 0% |
| 5 to 14 | 13±3% | Hyperthyreoidism, Graves' disease | 35% to 60% |
| Average | 12±4% | Colloid adenoma | 3% |

In adults the uptake and excretion of $I^{131}$ may be usefully measured. Less than 10% pick-up indicates hypothyreoid function, 15% to 30% is normal, while over 40% shows hyperthyreoidism, the tests being carried out at forty-eight hours. In Table III readings are higher, as the readings have been taken at twenty-four hours.

Radioactive iodine has proved useful in the treatment of primary Graves's disease, but it is too early yet to state what place radioactive iodine will ultimately hold. It is not indicated in nodular forms of goitre. Doses of four millicuries (rarely six millicuries) are given after a preliminary tracer dose to test pick-up. The immediate effect has been satisfactory, but it is too early to assess the ultimate results. Remissions are produced within four to eight weeks, and transient complications of tracheitis with cough, thyreoiditis with tenderness, increase of toxicity and hypothyreoidism have been noted. Quimby reported to the American Association of Physicians seven cases of primary thyreotoxicosis, in all of which satisfactory remissions occurred; but only 11 of 16 patients with recurrent toxic goitre had remissions. Soley and Miller[8] reported that 25 of 33 patients with Graves's disease responded satisfactorily within four months to treatment with radioactive iodine.

*$I^{131}$ in Carcinoma of the Thyreoid.*

With the onset of anaplasia the capacity of thyreoid cells to take up iodine diminishes. In *carcinoma simplex* there is little tendency for any to be taken up, but in the adult adenocarcinoma types some of this function may persist; but take up by carcinoma cells is the exception rather than the rule. Thus, on test, the total take up by the thyreoid gland is usually found to be diminished. If the tumour and its secondary deposits do take up iodine, this capacity may be utilized for the administration of a massive dose of irradiation.

The total removal of normal thyreoid in a carcinomatous patient with secondary deposits causes an immediate state of hypothyreoidism. In the subsequent month or two malignant deposits may, but do not always, show metaplasia with resumption of some of the thyreoid function, which is indicated by an increased capacity for taking up iodine. The onset of this metaplasia may be stimulated by the administration of pituitary thyreotropic hormone if available.

TABLE III.

*Thyreoid Gland Uptake and Urinary Excretion of $I^{131}$.*

(*After* Quimby.)

| Condition. | Average Percentage in Gland at 24 Hours. | Average Percentage Excretion in 24 Hours. |
|---|---|---|
| Normal thyreoid | 21 | 52 |
| Toxic goitre: | | |
| (*a*) Diffuse | 64 | 17 |
| (*b*) Nodular | 52 | — |
| (*c*) Exophthalmic | 57 | 22 |
| Non-toxic nodular | 19 | 50 |
| Hypothyreoidism | 3 | 62 |
| Carcinoma of the thyreoid | 14 | 58 |
| Acromegaly (hyperpituitrism) | 18 | 53 |
| Symond's syndrome (hypopituitrism) | 11 | 70 |

Thus it is being advised that a local thyreoidectomy should be carried out with removal of as much as possible of the thyreoid gland. Then one should wait eight to twelve weeks, during which time the hypothyreoid state may be somewhat relieved if secondary deposits assume any function. Then the scanning test should be repeated to see if any alteration has occurred. If so, a further therapeutic dose of iodine should be given.

The thyreoidectomy preferably should be surgical; but if this is not practicable, a medical "thyreoidectomy" with thiouracil, for example, or an irradiation "thyreoidectomy" with a therapeutic dose of $I^{131}$, should be carried out as the first step in treatment.

The therapeutic dose is calculated on oral administration of one millicurie of $I^{131}$ per gramme of thyreoid tissue. But first a small dose of three or four millicuries is given to put any residual normal thyreoid tissue out of action, and the risk of a subsequent crisis from the large following dose is minimized. Thirty or forty millicuries are then needed for the cancericidal dose; but if massive secondary deposits are present more must be administered, after an estimation, with radiological assistance, of total volumes of neoplastic deposits.[9] Large doses do not harm the blood-formative tissues, as little localization occurs in tissues other than thyreoid. The limiting factors of dosage appear to be the kidneys, in which irradiation of renal parenchyma during excretion may produce ultimate damage; these facts are not yet known, nor has time been available to determine what remote biological effects of damage may appear.

Unfortunately cases of carcinoma of the thyreoid are uncommon in which there is still sufficient residual capacity for picking up quantities of iodine likely to be enough to give adequate lethal irradiation to the cells. The efforts to stimulate increased iodine take up by the tumour cells will be watched with very great interest.

### THE SIMILARITY OF EFFECT PRODUCED BY CERTAIN DRUGS AND BY IRRADIATION ON GROWING CELLS.

The earliest medical writings contain records of the use of certain alkaloids and metallic poisons in the treatment of malignant tumours. Arsenic is the only one of these substances which has survived and which has been shown to have any direct effect on the multiplication cycle of cells. More recently colchicum and urethane have been shown to possess properties similar to arsenic. All these substances possess the power of non-specific inhibition of mitosis; but podophyllin, colchicum and urethane in addition exhibit the capacity of stimulating differentiation in the progeny of cells of the basal layers of multiform tissues. Arsenic is still occasionally used in the leuchæmias and in Hodgkin's disease, but its external use has been abandoned. Podophyllin has considerable power of inhibition of mitotic activity, but its toxicity renders it unfit for therapeutic use. Urethane was tried in the treatment of carcinomatosis, but it produced little effect on the neoplasm, though a profound leucopenia resulted. As a result of these observations of Edith Paterson, urethane has been successfully used in the treatment of the chronic leuchæmias.[10]

Urethane is without effect on *polycythæmia vera*; but it causes diminution of white cell counts to within normal limits, restoration of hæmoglobin levels and diminution of splenomegaly, hepatomegaly or gland enlargements in responsive cases of chronic leuchæmia. The results appearing are primarily due to the "specialization" effect, the most primitive cells showing the greatest changes; but also a "direct" effect causes a diminution of production of cells. This change is probably small in proportion to the specialization effect, and unlike radiation therapy, no delayed inhibition of mitoses is seen, so that treatment must be carried out almost continuously. The results in comparable cases of leuchæmia treated with X rays or chemotherapy favour irradiation as the early primary treatment; but the pharmaceuticals have a place in the later stages when diffuse marrow failure threatens.

Mustard gas became widely known as a vesicant during the first world war. It is a lipoid-soluble substance readily entering into the cells, and probably causes its effects by inactivation of specific enzyme systems. But it has another direct effect in inhibiting mitosis. The repair of damage caused by its action may there be delayed. The effects of the gas are those of vesication of superficial tissues, particularly cornea and skin; it produces gastro-intestinal changes with diarrhœa, and hæmoconcentration and convulsions occur as sequelæ.

Small doses of the gas cause a direct inhibition of mitosis in the resting stage, and in larger doses gross nuclear fragmentation is apparent. Genetic effects resulting in lethal or non-lethal gene mutations are produced. Thus the effects are comparable to those primary changes ascribed to irradiation, namely: (*a*) a photochemical destructive effect on cell protein; (*b*) a direct and specific effect of growth inhibition; (*c*) genetic mutations; (*d*) production of specialization in anaplastic cells arising from multiform tissues.

Numerous chemical substances of closely allied type have been therapeutically tested. Mustard gas is a member of the chlorethyl-sulphide family, but the chlorethyl-amines or nitrogen mustards are the preparations used for therapeutic purposes. Much work is being carried out, particularly at the Memorial Hospital, in the investigation of therapeutic properties of this family of chemicals.[11]

No useful results have been obtained in the control of cancer by and large. The greatest benefits have been obtained in certain of the reticuloses, and the results and indications for the use of nitrogen mustards closely parallel those for the administration of radioactive sodium or phosphorus.

These chemicals have been used purely for research studies, and conditions of suitable type have been treated solely by these means, *ab initio*, not always to the best interests of the patient. The indications for their use can be determined now from the available experimental material. In the acute leuchæmias no useful result is obtained. Good remissions may be obtained in the chronic leuchæmias and masses of glands or enlarged viscera may recede; but the duration of the remission is shorter than that obtained by radiation therapy. Blood counts fall with changes moving in the direction of restoration of hæmoglobin level and differential counts to normal. The effects on gland or visceral masses are particularly transient, and the presence of such deposits or infiltrations indicates the use of accepted forms of radiation therapy. Nitrogen mustards, like isotopes, therefore have their indication when marrow function is failing—a stage which cannot be much helped with X-ray therapy. The mustards are therefore indicated, not at the commencement of treatment, but in the later stage.

Similar conditions apply to their use in Hodgkin's disease. In the early stages it is still best controlled with irradiation, as the dramatic recessions of tumour masses under mustard therapy may be very transient, with recurrence perhaps in two or three weeks. X-ray therapy should therefore be used as heretofore until such time as residual gland masses fail to show response to irradiation, at which stage the glands usually exhibit the third histological phase of fibrosis. At the same time infiltration of marrow, or lung or bone deposits, may be present with gross anæmia. Administration of nitrogen mustard is then indicated, and if a response is obtained, X-ray therapy may be again administered with prospect of a response as seen in the earlier stages. The simultaneous administration of X-ray therapy and nitrogen mustards produces no augmentation of effect, rather the reverse.

Evidence of marrow failure and resistance to X-ray therapy therefore constitute the prime indications for the use of nitrogen mustards.

In lymphosarcomatosis results are not much more promising, but a proportion of worthwhile remissions is obtained. Multiple myelomatosis and diffuse neuroblastomatosis have not responded to treatment. The drug is not worth while in the great group of epithelial neoplasms, though occasional benefit has been obtained in diffuse melanomatosis and in carcinoma of the lung.

Administration is not without risk. The administrator should protect his eyes and hands, and the care of the exposed skin of the patient is necessary. Thrombosis and subsequent phlebitis at the injection site are common complications, which probably can be avoided by introducing the mustard through an intravenous saline solution system instead of by direct intravenous injection. Nausea and sickness commonly follow two to six hours after administration, and splenic infarction follows the introduction of large increments of dosage. Treatment must be pushed till leucopenia is produced, and therefore regular hæmatological control is essential during the course. The effects are transient, the courses must be repeated, and on repetition less satisfactory results are to be expected.

The drug undoubtedly has its greatest use in the late stages of Hodgkin's disease, and it has a place in the palliation of some forms of advanced cancer.

### HANDLING AND ADMINISTRATION OF ISOTOPES.

Unstable isotopes are radioactive and therefore must be handled with full radiotherapeutic protection technique. Risks exist therefore to the administrator, to the patient and to the hospital staff if carelessness involves contamination of hospital laboratories, apparatus, wards or utility rooms. The risk increases greatly with the increasing half-life of the isotope and contamination; for example, the presence of $C^{14}$ with a half-life of 5000 years means permanent radiation in the room.

A special administration room should be set apart. The staff should wear changeable gowns and gloves, and tin trays with sterile disposable absorbent paper should be used instead of towels. Isotope solution should be coloured for easy recognition. All syringes and glassware should be used only for the particular purpose, and special decontamination procedure for cleansing should be carried out. Oral or intravenous administration techniques are specially designed to avoid any possible contamination. It is justifiable to regard an isotope solution as of the same danger as a culture of virulent bacteria.

In the ward special precautions may need to be taken about collection and disposal of excreta and decontamination of utensils.

If scanning or tracer tests are carried out, the counters should be in a room separated from the isotope administration room. Any room contamination will be likely to increase the background count rate, which normally is chiefly due to cosmic rays. Avoidable sources of errors can be eliminated by the use of the extra room.

Administration laboratories should be "monitored" after use to test for possible contamination.

Waste radioactive substances or contaminated materials should be placed in an outside "grave" until such time as decay of radioactivity has occurred. This is a matter of impossibility in the case of carbon. But enough has been said to show that extreme care is essential in the handling of these substances.

ACKNOWLEDGEMENTS.

I have spoken in this address of my personal findings as a result of meeting workers in various centres which I visited in the United States and in Great Britain. I have not attempted to review the literature in the fields of discussion. If errors are present, the faults lie with my recording of the details given to me in the clinics and laboratories, and the workers are not to blame. For interest I have sometimes recorded their names with the details of information which I gathered. Here I must express my gratitude to the many people who were only too willing to help me with the fruits of their personal experiences: Dr. Reinhard and Dr. C. V. Moore in St. Louis; Dr. Pendergrass, Dr. R. Chamberlain and Dr. Schiffer, Dr. Edward Chamberlain, Professor Swensen and Dr. Lowell Erf at Philadelphia; and in New York Dr. Edith Quimby, Dr. J. J. Nickson and Dr. Rubenfeld. All these gave me much assistance in my investigations into the uses of the isotopes. Dr. Karnofsky and Dr. Burchenall, of the Memorial Hospital, put much information about the mustards at my disposal. Dr. Edith Paterson and Dr. Thomas showed me their clinical work with chemotherapeutic substances at Manchester. To all these workers I express my grateful thanks for personal considerations extended to me.

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## A SELF-RETAINING ABDOMINAL RETRACTOR.

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A SELF-RETAINING abdominal retractor[1] is herein described which has been in constant use and subjected to many modifications during the last sixteen years. It was originally (in 1931) modelled on one being designed by Dr. Hugh Trumble while the writer was his house surgeon. Shortly afterwards, this writer departed from Dr. Trumble's "sphere of influence", and in the subsequent years made various modifications and improvements on the original. However, the debt owing to Dr. Trumble for the basic idea is gratefully acknowledged.

[1] The name of the supplier is obtainable from the author.

### Description of the Apparatus.

The apparatus consists of a thin circular steel ring, ten inches in external diameter and wedge-shaped in section, and a series of retractors and hands which may be fixed temporarily but firmly to the ring by means of a sliding locking piece (Figure I). The ring is smooth and very slightly concave on its upper horizontal surface and slightly roughened and flat on its lower inclined surface. The plane of each makes an angle of 8·5° (Figure I).

The side and suprapubic retractors are for the retraction of the wound edges and are of orthodox design. Special care has been taken in designing them to ensure that the lateral edges do not cut into the tissues, this being attained by the provision of a full curve at these margins (Figure I).

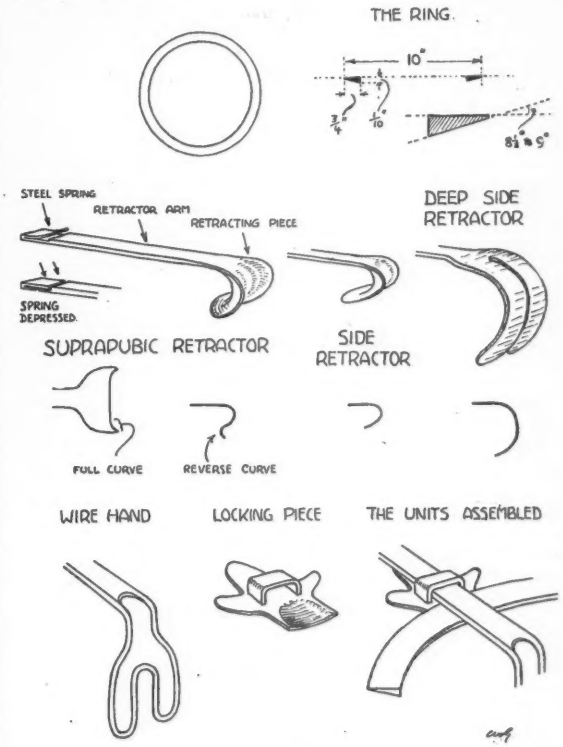


FIGURE I.
Showing the components of the apparatus.

The side retractors, two in number, are used for retracting the edges of the incision and are those first applied.

The suprapubic retractor is most commonly used at the lower angle of subumbilical incisions. There is a pronounced reverse curve at the deep edge to prevent sharp pressure on the bladder.

The deep side retractors are of sheet copper and are for use, in place of the usual side retractors, when the abdomen is unduly obese. They are bent at the time of application to fit the patient. Irrespective of the degree of obesity, one of these retractors, suitably bent to project well under the abdominal wall, is of considerable value in the upper lateral angle of the left oblique incision for operations in which approach to the splenic flexure of the colon is necessary. If the ring is lifted away from the patient, this retractor provides a broad surface on which the lateral abdominal wall can be raised.

The retracting pieces of the wire hands are constructed of soft copper wire bent to various shapes, the wire being brazed onto the retractor arm. These are described in detail later.

The retractor arm is of strip steel of rectangular cross-section, 0·6 inch by 0·1 inch, the length being between five and six and a half inches, according to the particular retracting piece attached. One end is brazed to the retracting piece and the other is recessed to accommodate a square of steel spring, which is attached by one edge only to the end of the retractor arm (Figure I). The slight curve in the spring is such that it normally projects above the plane of the top of the retractor arm. The hole through the locking piece allows the latter to slide easily but snugly along the retractor arm. The locking piece is slipped onto the desired retractor arm by means of gentle pressure which depresses the spring sufficiently to allow the locking piece to slide over it. It can then slide freely along the arm, but cannot fall off owing to the upward projection of the free edge of the spring. When required, it may be readily slipped off by pressing, between the thumb and fingers, the spring edge down to the plane of the retractor arm upper surface (Figure I).


FIGURE II.
Showing the method of attaching the retractor to the ring.

Each of the locking pieces (Figure I), of which eight are supplied, consists of a shaped piece of sheet steel with a curved piece brazed onto its top surface in such a way that a slot is formed through which the retractor arm may slide easily. The sheet is not flat. It possesses slight curves in two planes so distributed as to ensure maximum fixation of the locking piece, retractor arm and ring to one another, as described later. The locking piece is slipped on to the desired retractor or hand by means of gentle pressure, which depresses the spring sufficiently to allow the locking piece to slide over it. The latter may then slide freely along the whole length of the retractor arm until it is stopped by impinging on either the upward projecting spring laterally or the retraction piece medially (Figure I). It may be readily slipped off the retractor arm by pressing between thumb and fingers the spring edge down to the plane of the retractor arm upper surface.

In the whole apparatus there are no screws or small parts liable to be readily lost, and no screw threads, ratchets, hinges or moving parts subject to wear. Cleaning and assembling are thus simple procedures.

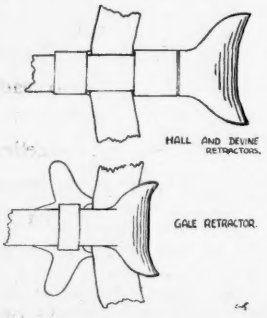


FIGURE III.
Showing the maximum degree of retraction obtainable with the Devine, the Hall and the present retractors.

## Technique of Application.

A median subumbilical incision being used as the example, the ring is placed over the incision with the smooth, flat, horizontal surface uppermost. A side retractor (or deep side retractor if the patient is obese) is inserted in the side of the incision nearest the surgeon and attached to the ring with the locking piece (as described later) and with the retractor arm crossing the ring at right angles.

The second side or deep side retractor is placed in the opposite side of the incision, and the wound edges are retracted by compressing the medial surface of the retractor and the outer edge of the ring on either side of the retractor arm between the thumbs and fingers of both hands (Figure IIA). When retraction is optimal the index fingers slip the locking piece down into firm contact with the ring (Figure IIB). The thumbs are transferred to the inner ring margin and the locking piece is firmly pressed into position (Figure IIc and Figure I). The pressure is exerted against the "spring" inherent in the three related structures—namely, the ring, the locking piece and the retractor arm. The whole success of the retractor is dependent on the firmness with which this act is performed.

The suprapubic retractor is then applied in a similar way to the lower end of the incision and the wire hands are attached in turn when and where required.

The wire hands are usually applied over carefully arranged gauze packs, but these may be omitted in the retraction of structures such as the liver. The side and suprapubic retractors operate better if care is taken to fix them at symmetrically opposed points on the ring, care being taken to prevent bowel from being inadvertently grasped between the retraction pieces and the abdominal wall. At times the optimal arrangement of a wire hand may be such that its arm has to cross the ring obliquely. Provided the obliquity is not too great, firm fixation can still be obtained.

The hands are released from the ring by twisting the outer end of the retractor arm from side to side in the same plane as the upper surface of the ring, this action being combined with pressure on a corner of the locking piece.

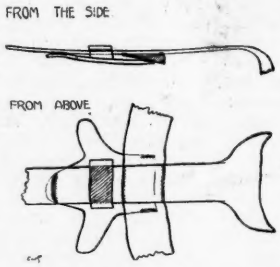


FIGURE IV.
Showing the features on which depend the firm fixation of the retractor to the ring. To facilitate visualization, all structures are to be regarded as transparent. The actual gripping surfaces can then be indicated in the lower figure by oblique shading, and in the upper figure by a thick line. For emphasis, all curves in the side view are exaggerated. Note the curve in the retractor arm after it has been fixed in position.

## The Special Features of Design.

Existing self-retaining retractors possess varying degrees of several deficiencies of design as follows.

1. They are not sufficiently simple. All surgical instruments requiring sterilization must be dismantled, cleaned and assembled by nurses possessing varying degrees of mechanical sense. It is quite simple for the designer of an instrument (who must be mechanically minded to be a designer) to handle a complex and perhaps delicate mechanical instrument; but the majority of surgeons and nurses are not mechanically minded. Design must therefore be guided primarily by this principle of mechanical simplicity. The Devine retractor frame has an adjustable side moved by two turnscrews operating a rack and pinion. If these screws are not turned in unison, the rack and pinion are apt to jam and this is a not uncommon experience. The frame itself requires assembling after cleaning, and this is apt to result in a part's being inserted back to front. The writer's retractor has no screws. It has no moving parts capable of jamming or being lost. It has no projections to entagle sutures.

2. Either the extent of retraction possible is restricted or, if it is adequate for large incisions, it results in too great an overall width of frame *plus* retractor arms. In the Devine[(1)] and Mervyn Hall[(4)] retractors the mechanism for locking the interchangeable retraction pieces to the retractor arms, by impinging against the inner margin of their frames, greatly restricts the range of retraction (Figure III). The greatest degree of retraction obtainable with each of the three retractors is as follows: Devine, five inches; Hall, five and a half inches; Gale, seven inches. The overall measurements between outer tips of retractor arms with such retraction are as follows: Devine, 23·5 inches; Hall, 20·5 inches; Gale, 20 inches. This is of importance in restricting the approach of the surgeon's and assistants' bodies to the patient's side. In this present retractor the retractor arm is attached by the maker to the

actual retraction piece in such a way that the plane of the under surface of the retractor arm is continuous with that of the adjacent retraction piece (Figure I). This allows the fully retracted unit to be fixed to the ring with part of the retraction piece lying on top of the latter (Figure IIIB). This arrangement allows the maximum retraction for the ring supplied.

3. The methods of fixing the arms to the frame possess undesirable features. The Devine retractor arms are intended to be locked in position by the wedging of the arm between the frame and an inclined plane on the under surface of a hook set into the frame. When the retractor is new this arrangement may operate satisfactorily; but in time wear occurring in the hook and in its attachment to the frame results in loosening of the hooks and disappearance of the "inclined plane" locking mechanism. From then on, fixation of the arm to the hook is dependent on maintenance of pull on the retractor towards the centre of the incision, this being supplied by the stretched abdominal wall. "There is a slight muscle pull on the wound retractors. It is this pull which keeps the retractors firmly jammed into the double hooks on the frame" (Devine[3]). Notwithstanding this statement, it is this writer's experience that as operation proceeds the abdominal wall slackens and the arms of the Devine frame frequently fall loose. The square design of the frame contributes to this disability.

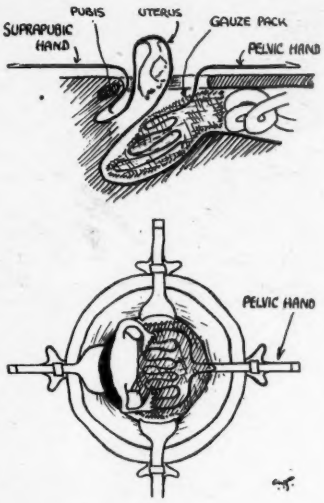


FIGURE V.

Showing arrangement of retractors and the "pelvic" hand in pelvic surgery.

The Hall retractor uses a locking piece which is wedged by the surgeon onto the ring where required. The retractor arm is then moved through a slot in this locking piece and is fixed in position by a ratchet incorporated in the latter. The Hall retractor thus uses a similar principle to that of the present retractor, but with one most important difference—namely, the "spring" inherent in the metal of the instrument is not utilized. As a result, as the operation progresses, the locking piece (and therefore the retractor arm) falls loose.

In the present retractor the natural "spring" of the retractor steel is utilized to the maximum. The features making for positive and persistent fixation of the retractor arm to the frame (that is, the ring) are as follows. (*a*) The top surface of the ring is slightly concave. This results in the retractor arm's gripping the ring edges only; this provides a better grip than a flat surface, which may possibly be convex in spots (Figure IV). (*b*) The under surface of the ring is roughened. (*c*) The angle of the wedge of the ring is so related to that of the locking piece, and the locking piece is so shaped, that when the latter has been pushed firmly into position its under surface grips the retractor arm and ring at three points only (see Figure IV). The "spring" inherent in the arm, the ring and the locking pieces between the various gripping points contributes greatly to the fixation of the arm. Provided one forces the locking piece firmly into position with the manœuvre described, the retractor arm rarely becomes loose during operation.

4. The mechanical "hands" possess limited applicability to varying patients and problems of retraction. In both the Devine and the Hall retractors each hand consists of rigid non-malleable wire twisted to a definite but unchangeable shape. In both an attempt is made to meet varying problems of retraction by having a large number of such hands available; but such a provision does not prove universally satisfactory.

In the present retractor the wire hands have certain features common to all, these constituting the most valuable characteristics of the apparatus. They are constructed of copper wire readily malleable by the surgeon. The thickness of the wire is carefully chosen to suit the particular function of each hand. The shape of each hand has not been haphazardly arrived at. Each has been evolved to subserve a definite function and to allow alteration of its shape in certain definite directions (Figure VII). Each is intended to be used as an instrument to be freely and ruthlessly bent into any shape that the exigencies of the operation may require. This provision of malleability and the encouragement of its utilization obviously mean that the hand is subject to wear and tear, and it should therefore be regarded as possessing a life as limited and variable as a forceps or scissors. In time the wire may break, according to the surgeon's preparedness to exploit its function fully. Such breakage is unavoidable; but sixteen years' experience indicates that this happening is most infrequent (occurring at intervals of years, not months), and should not be consciously avoided at the expense of getting the most out of the retractor's possibilities.

*The Hands.*

Each hand may be readily bent by the surgeon's gloved fingers in at least four directions. (i) Its area and lateral shape can be altered by compression or extension. (ii) Its convexity or concavity may be varied. (iii) The angle between its plane and that of the under surface of the retractor arm can be changed. (iv) The angle between its plane and that passing vertically along the side of the retractor arm can be varied.

The spot most vulnerable during this moulding is the junction between the malleable wire and the rigid retractor arm. Careless moulding will result in the initial bend's always occurring at this spot. With care this junction can be protected and the alterations established with a gentle curve extending over an appreciable length of the wire just beyond this spot. With reasonable care breakages should be separated by intervals of years. However, all hands are readily replaced or repaired. It is now the writer's practice to have a break in the wire repaired at a garage by brazing. The broken ends are placed together without overlap, a touch of brass is applied, and the area is smoothed with emery cloth. The repair takes only a few minutes.

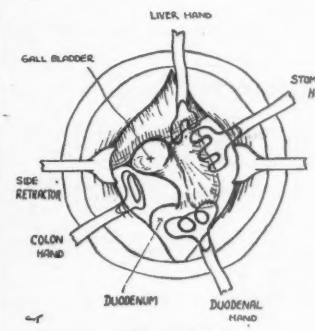


FIGURE VI.

Showing the arrangement of the hands for gall-bladder surgery.

The pelvic hand (Figures VII and V), the most useful of this series, is used in all abdominal gynæcological procedures. The side and suprapubic retractors having been applied and the patient placed in the Trendelenburg position, the assistant lifts and holds the uterus out of the lower angle of the wound and lifts the upper margin of the ring away from the abdominal wall. The surgeon, on the patient's left, displaces the intestines and omentum into the upper part of the abdomen, applies a large scarf over their surface so that the scarf dips well to the bottom of the pouch of Douglas, and then applies the pelvic hand over the scarf and attaches it in the mid-line to the cranial margin of the ring. The pelvic hand is shaped by

the surgeon so that its plane approximates that of the upper part of the sacrum, and it is drawn cranially so that its lower end presses back towards this bone. Just before the hand's insertion into the wound, its width, concavity and depth have also been adjusted by the surgeon after a rapid appraisal of the pelvic dimensions and shape. After fixation to the ring the lateral angles are bent if required and the scarf margins tucked in to keep the caecum and any stray ileal coils out of the way. The uterus and adnexæ are thus isolated and rendered accessible (Figure V). If the operative procedure is such that this hand is unsuitable, as in recto-sigmoid operations, one or more of the other wire hands is used. The pelvic hand as originally supplied is shaped as in Figure VII;

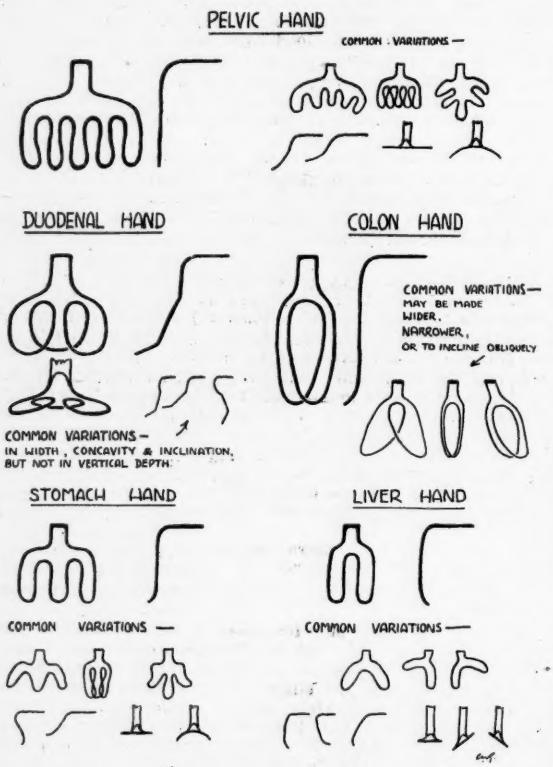


FIGURE VII.
Showing the wire hands and the variations in shape to which they are commonly subjected.

but with continued use its symmetry becomes lost as a result of the various manipulations to which it is subjected.

Full-size diagrams of the original shape of all hands are supplied with the retractor, to enable the surgeon periodically to restore the original shape of the hands if he so desires. In doing so, the fingers should be used wherever possible. Pliers may produce cuts in the wire at which breakage may later occur. The original shape, with common variations, of each of the various hands is shown in Figure VII.

The colon, duodenal, stomach and liver hands are primarily used to retract the organs indicated by their names and in operations on the biliary tract. They are also used in any situation where their shape and size might suggest their suitability. In cholecystectomy, through a right upper paramedian incision, the side retractors are placed as in Figure VI. The gall-bladder is grasped and held up and to the right, and its adhesions, if any, having been divided, the omentum, small bowel and pylorus are displaced down and to the left (this being facilitated by lifting the ring), a scarf is placed over them, and the duodenal hand is placed to retract these structures towards the 5 o'clock position on the ring, this hand at the same time being shaped and arranged so as to put the hepato-duodenal ligament on the stretch. The most common moulding used with this hand is alteration of the angle between the plane of the wire and that of the under surface of the retractor arm (Figure VII). The colon hand is applied at the 8 o'clock position to hold the hepatic flexure of the colon away from the gall-bladder. The most common moulding for this hand is to twist the wire near its attachment to the retractor arm in such a way that when it is in position its tip inclines slightly cranially as well as backward (Figures VI and VII). The stomach hand is next applied at the 2 or 3 o'clock position to hold the stomach to the left. In some cases a liver hand moulded appropriately may prove more suitable in this position. Finally, a liver hand is freely moulded and placed to retract the liver where it appears most advantageous. The liver hand is purposely made relatively delicate (and of thin wire), and is intended to be freely bent in all directions. As the operation progresses, indication for alteration of shape, size or position of one or more of the hands may appear. At the stage where the common bile duct is to be probed it is usually desirable to remove the duodenal hand. The steps of the procedure are thus as described so fully by Devine.[1]

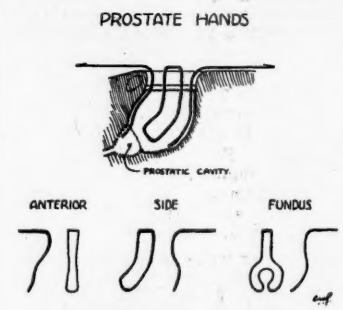


FIGURE VIII.
Showing the hands used in suprapubic prostatectomy.

The prostate hands consist of a right side hand, a left side hand, a fundus hand and an anterior hand (Figure VIII).

The side hands are so shaped as to incline back and down towards the prostatic cavity, and to allow of being bent to suit abdominal walls of varying thickness.

The fundus hand is of thin wire to allow ready moulding if required, and may be made wider, narrower or more curved.

The anterior hand is shaped so that its extremity will hold the anterior part of the prostatic cavity forward and well open.

Repeated use of the various hands in the foregoing operations rapidly makes the surgeon familiar with their potentialities. They are consequently found of use for purposes other than those indicated by their names. The deep side copper retractor, adequately bent, is of considerable value in the approach to the splenic region as described. Careful application of gauze packs is a necessary preliminary to the proper application of the wire hands. Rearrangement of hands and perhaps the use of the other hands at later stages in the operation contribute to the usefulness of the apparatus.

## Conclusion.

The apparatus has stood the test of sixteen years' constant use and has obviated the need for an assistant except in the rarest of instances. With its help; high gastric resection, common bile duct surgery, duodenectomy and pancreatectomy, and the deepest of pelvic manipulations have all been performed with no difficulty of access.

## References.

(1) H. Devine: "The Surgery of the Alimentary Tract", 1940, page 325.
(2) H. Devine: *Loco citato*, page 330.
(3) H. Devine: *Loco citato*, page 341.
(4) M. Hall: "An Operating Frame on a New Principle", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, 1943, page 164.

# Reports of Cases.

## A CASE OF TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN.

By MARTHA RENTH, M.D. (Vienna),
*From the Tuberculosis Annexe, Queen Victoria Hospital, Melbourne, and the Neurological Department, Alfred Hospital, Melbourne.*

IN view of cumulative evidence that tuberculous meningitis is one form of tuberculosis in which the use of streptomycin is indicated, and because of the unusual clinical course and the interesting pathological findings, this case is presented.

### Clinical Record.

Mrs. A.W., a *multipara*, aged thirty-six years, and five months pregnant, was admitted to the obstetrical unit of the Queen Victoria Hospital. Four days before her admission to hospital slight vaginal hæmorrhage had begun, and on the day of her admission lower abdominal pain developed. For two days she had also had pains in the right side of her chest on breathing.

On her admission to hospital her temperature was 101° F. (in the morning). Clinically, the heart and lungs were clear. A miniature radiograph of her chest had been passed as revealing no abnormality six weeks previously.

The fœtus and placenta were delivered on the day of her admission to hospital, but the next day the patient had a cough and an evening temperature of 105° F. Although the lochia were not offensive, the presence of a septic process was presumed, and the administration of sulphadiazine and of penicillin was started. Post-vaginal material yielded no cultures of pathogenic organisms, and the temperature continued to swing.

Nine days after the patient's admission to hospital, an X-ray film of the chest was reported on as follows: "Vague mottling throughout both lungs; some confluent areas at the bases, where there is also some pleural reaction. Appearances suggest bronchopneumonia with some pleural reaction." A test for cold agglutinins yielded a negative result. The Mantoux test with a dilution of 1:1000 produced a positive reaction. The temperature did not change materially during the next three weeks, and the patient developed night sweats.

X-ray examination of the chest after three weeks revealed the following findings. The appearances in the chest had not appreciably changed; fine mottling was present throughout both lungs with considerable pleural reaction at the base of the right lung. The lesions were slightly harder than before, and the radiologist considered that the possibility of miliary tuberculosis had to be considered. A blood count four days later showed that 17% of the leucocytes were eosinophile cells, and the possibility of an eosinophilic pulmonary condition was considered. One week later, however, the result of a differential leucocyte count had changed to the presence of 22% of monocytes and only 1% of eosinophile cells; this indicated a significant change—from an allergic response to infection to tubercle formation.

At this stage the patient developed fairly severe and frequently recurring abdominal pains, which reappeared throughout most of her illness. She was examined by a gynæcologist, who diagnosed tuberculous peritonitis, endometritis and salpingitis. Culture of cervical pus yielded a growth of *Mycobacterium tuberculosis*.

Twenty days after her admission to hospital the patient had double vision for about half an hour, and lumbar puncture yielded clear cerebro-spinal fluid under normal pressure. The chemistry of the fluid was normal, and four cells were counted per cubic millimetre.

A diagnosis of miliary tuberculosis was established beyond doubt by the discovery of acid-fast bacilli in a smear of a twenty-four hour specimen of urine.

At that time streptomycin could not be procured in adequate quantities for therapeusis, and during the next two months the patient's condition remained unchanged. Ten weeks after her admission to hospital, however, she developed right facial paralysis of the lower motor neuron type, course nystagmus to the left, and fine nystagmus to the right. Lumbar puncture yielded clear cerebro-spinal fluid under normal pressure. The response to the Queckenstedt test was normal. The fluid contained 50 milligrammes of protein per 100 millilitres, 644 milligrammes of chlorides per 100 millilitres, 40 milligrammes of sugar per 100 millilitres and two cells per cubic millimetre. She developed increasingly severe headache and blurring of the left optic disk and hypodiadochokinesis of the right hand, and Babinski's sign was present on the right side. One month later the cerebro-spinal fluid was under increased pressure, and on lumbar puncture was found to contain 77 red blood cells per cubic millimetre; guinea-pig inoculation produced post-mortem signs of active tuberculosis.

Four months after the onset of the illness streptomycin became available; 0·25 gramme was given intramuscularly

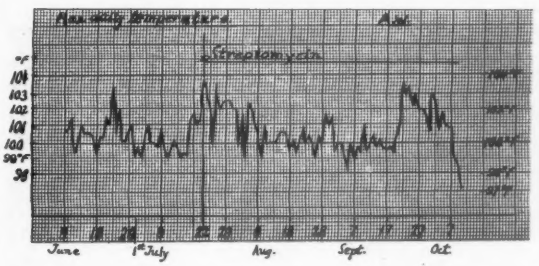


FIGURE I.

every four hours, to a daily total of 1·5 grammes, and 100 milligrammes were given intrathecally every second day.

For the next four days her headache increased in severity, she vomited nearly continuously, and she had to be given fluids by the rectum. Bilateral papillœdema was observed.

On the fifth day she felt better, her headache had decreased and she retained fluids given orally; from then on her condition continued to improve. The temperature fell, headache was so slight that it did not require medication, and the right optic disk became normal. Examination of the left disk revealed slight blurring of the upper and nasal edge. Apart from a slight sagging of the right corner of the mouth, the right facial nerve recovered full function. The patient was bright and happy, was able to read and wanted to start handicraft.

This improvement lasted for six weeks, when she again developed increasingly severe headache and retention of urine. Papillœdema now increased, the right pupil became dilated and nystagmus reappeared. The cerebro-spinal fluid pressure was 270 millimetres of water; the fluid contained 53 leucocytes per cubic millimetre, of which 67% were mononuclear cells. The chloride content was 633 milligrammes *per centum* and the protein content 140 milligrammes *per centum*.

She became drowsy, and eight weeks after the start of the treatment, for the first time developed neck stiffness. For two days she exhibited a phenomenon which we were unable to explain: her pupils reacted promptly to light, but with dilatation, yet normally to convergence. Treatment was continued as before, but her condition deteriorated in a manner usual to untreated tuberculous meningitis. Shortly before her death, lumbar puncture revealed an incomplete spinal block, which was attributed at the time to the development of internal hydrocephalus from inflammatory exudate—an assumption which was disproved by the post-mortem findings. As will be seen from the pathological notes, it was due to a condition

which could hardly have been diagnosed under the circumstances.

Application of streptomycin was continued by the cisternal route and by intramuscular administration.

The patient died eleven weeks after the start of treatment, twenty-three weeks after the appearance of the first cerebral symptom, and twenty-six weeks after the beginning of her illness. A total amount of 119 grammes of streptomycin had been given intramuscularly and 2·9 grammes intrathecally. At no time were there any eighth nerve symptoms which could have been attributed to streptomycin.

### Autopsy.

Autopsy was performed twenty-two hours after death, and revealed typical miliary tuberculosis of lungs, kidneys and spleen, and tuberculous peritonitis, salpingitis and endometritis. A typical Ghon's focus, consisting of two caseous nodules in the posterior parts of the lower lobe of the right lung subpleurally, was found and considered the primary focus.

The brain and spinal cord were removed extradurally and hardened in formalin.

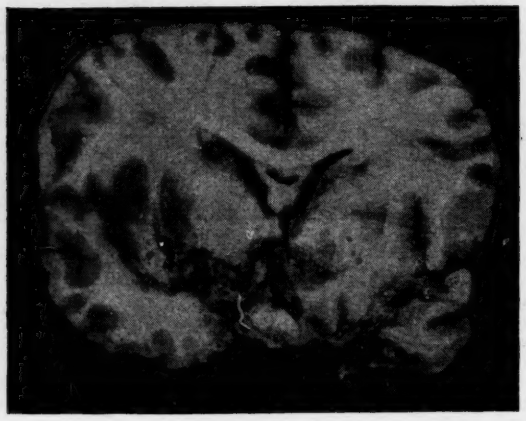

FIGURE II.

Coronal section showing tuberculous exudate at the base of the brain invading the hypothalamic area, the chorioidal fissures and the posterior horns of the ventricles.

### *Pathological Examination.*

I am indebted to Dr. L. B. Cox for the following pathological notes.

The brain, removed extradurally, and the spinal cord had been fixed in formalin. No significant changes were observed in the uncut brain other than partially organized exudate at its base. This surrounded the chiasma, the infundibulum and the third nerves, and extended well down the anterior surface of the pons.

Coronal sections showed the tuberculous process to have involved the floor of the third ventricle. Laterally it extended into the recesses between the peduncles and temporal lobes, particularly on the left side, where the chorioidal fissure was greatly distended. Anteriorly it reached the Sylvian fissure, but macroscopically it did not seem to extend along it. It surrounded optic nerves, chiasma and tracts, and the upper surfaces of the oculomotor nerves. The cortical surfaces of the hemispheres and cerebellum did not appear greatly involved. Nowhere was caseation macroscopically visible.

The ventricles were not dilated, and except for the third and temporal horn of the left lateral ventricle, perhaps, did not seem involved. No exudate could be distinguished in the cerebello-pontine recess, or about the cerebellum. In the left half of the mesencephalon was a small ovoid mass measuring three by two millimetres in transverse section, which was regarded as a tuberculoma.

The spinal cord and membranes seemed normal except in the mid-dorsal region. Here, the posterior part of the cord was distended by a rounded mass involving from three to four centimetres of its length, which was wrongly regarded as a tuberculoma. It seemed that it might have caused at least a partial spinal block.

### *Microscopic Examination.*

Sample sections from brain and cord were embedded in paraffin and stained with hæmatoxylin and Van Gieson's stain. All sections were examined for tubercle bacilli by the fluorescence method by Mr. Glen Buckle.

The cerebral and spinal subarachnoid spaces contained exudate over the cerebral cortex and spinal cord, which was grossly present in the basal cisterns and in the chorioidal fissures. It was cellular, consisting largely of lymphocytes and large mononuclear cells. No giant cells were observed. In the area of greatest involvement, the basal cisterns, there was pronounced arteritis, with epithelioid cell systems about the vessels, and round-cell infiltration and connective tissue formation in their

FIGURE III.

Coronal section showing small healing tuberculoma at the junction of pons and mesencephalon.

adventitiæ. In places their endothelium had so overgrown as to fill the lumina with a spongy tissue, of which the interstices contained red blood cells. The meninges were thickened and there was much fibrinous exudate in the cisterns.

The inflammatory process had involved the base of the brain. The hypothalamus was grossly disorganized, with areas of round-cell infiltration, arteritis and caseation, and accumulations of polymorphonuclear leucocytes. Tubercle bacilli were abundantly demonstrated. The inflammatory process extended to the entire ependymal lining of the third ventricle.

The exudate over the surface of the cerebral hemispheres contained lymphocytes and large mononuclear cells, and was particularly prominent in the sulci. The surface of the brain was not seen to be invaded, and the deeper intracerebral vessels were not surrounded by inflammatory cells. Tubercle bacilli were demonstrated in the subarachnoid space.

The small suspected tuberculoma within the mesencephalon proved to be a caseous area enclosed within a firm connective tissue sheath containing many lymphocytes. No giant or epithelioid cells were found, and no tubercle bacilli. It was thought to be a tuberculoma in the stage of healing.

The spinal subarachnoid space contained cellular exudate, but the cord itself did not seem to have been invaded, although sub-pial œdema was observed in some sections.

Arteritis, when present, was mild, although perivascular infiltration with lymphocytes was common, particularly in those vessels related to the spinal nerve roots. One small epithelioid cell system was found superficially in a nerve root of the *cauda equina*.

The presumed tuberculoma of the mid-dorsal region proved to be a congenital malformation, consisting of a central angiomatous mass and heterotopic masses of grey matter containing many nerve cells, enclosed by concentrically disposed glia. Two small islands of grey matter with neurons were also observed further dorsally, all being derived from malformation of one posterior horn. The distension from this mass, with the further slight distension of the subarachnoid space attendant upon the tuberculous process, could have caused a partial spinal block. No tubercle bacilli were demonstrated in sections of the brain stem and spinal cord.

### Conclusions.

There was pathological evidence of some healing of the tuberculous process, as shown by the small tuberculoma of the brain stem, and by the absence of tubercle bacilli from the spinal subarachnoid space of sample sections. Cerebro-spinal fluid circulation was not obstructed, and except in the final stages of partial spinal block, streptomycin could have gained entrance to the ventricles when introduced intrathecally by the spinal route. Nevertheless, the caseous area about the third ventricle would hardly have allowed its diffusion in that site, and this area, unless adequately encapsulated, would have been a possible source of reinfection of the subarachnoid space.

Examination of this brain again reinforces the lesson that early treatment rather than dosage is responsible for good results in tuberculous meningitis, and it remains a matter for speculation whether this patient, whose treatment was started four months after the onset of the illness, could have been saved by a prompt application of streptomycin. More recent work, on the other hand, has established the fact that tubercle bacilli rapidly acquire resistance to streptomycin, and this may well have been a contributing factor to the fatal outcome of this case. There seems to be no doubt, however, about the facts that the progress of the illness, which when untreated progressed inexorably, was at least temporarily halted, with great subjective and objective improvement in the patient's condition, and that her life was prolonged by several weeks.

### Acknowledgements.

I wish to thank the superintendent of the Queen Victoria Hospital, Dr. Joan Grainger, for permission to publish this case, and for help; the dispenser of the Queen Victoria Hospital, Miss Mary Burgess, for her ready cooperation; Dr. L. B. Cox for the pathological notes; and Mr. Glen Buckle for his technical assistance.

## Reviews.

### DISEASES OF THE CHEST.

THE first edition of Dr. Robert Coope's treatise of "Diseases of the Chest" was noticed in this journal on January 27, 1945.[1] The favourable opinion which we then expressed has evidently been widely shared, for there have been two further impressions of the first edition since then and the book now appears, entirely reset but very little altered, in a second edition. A valuable addition is the description of the anatomy of the bronchial tree in the chapter on applied anatomy and physiology; this is now illustrated with many diagrams, based on the work of Foster-Carter and Hoyle, showing the location in X-ray films of shadowing due to consolidation in the several broncho-pulmonary segments. Also, helpful new diagrams illustrating the effects of deflation of these segments have been introduced into the chapter on pulmonary collapse. Other alterations are of a very minor character, such as the substitution, in the diagram of a poultice applied to the chest, of a jolly-looking fellow for the lugubrious creature depicted in the first edition.

[1] "Diseases of the Chest: Described for Students and Practitioners", by Robert Coope, M.D., B.Sc., F.R.C.P., with a foreword by Lord Horder; Second Edition; 1948. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5½", pp. 558, with illustrations, some of them coloured. Price: 25s.

### RECENT ADVANCES IN SURGERY.

"RECENT ADVANCES IN SURGERY" by Harold C. Edwards, of King's College Hospital, is really just what the author has pictured it to be in the preface: "a series of snapshots in words, of current surgical practice".[1] These snapshots suffer the defects of the instantaneous picture of a moving scene, but they do give the reader a clear and concise view of the surgical scene as the advance reaches a given point, and that is the most such a publication can hope to do.

The early chapters deal with the subjects of wound healing, shock and associated conditions, and antibacterial therapy. The last subject is dealt with rather too lightly, as it is likely to be one of the most important for many of the readers whom this book is intended to help. The following section deals with recent work on the surgery of the alimentary tract and one of the clearest pictures is given of the present writings on the repair of inguinal hernia.

The section on the thorax is contributed by R. C. Brock and a particularly good chapter is devoted to the surgical treatment of bronchial carcinoma. D. W. C. Northfield, of the London Hospital, covers the field of neurosurgery and one of the fullest sections is devoted to a discussion on posterior protrusions of the intervertebral disk. Radiotherapy in malignant disease is discussed by Sir Stanford Cade.

The book is produced in a practical and attractive style; the subject matter is well set out and there is generous inclusion of illustrations. One of the most useful features is the list of references given at the end of each chapter. These references to valuable articles provide the reader with a sound list of original contributions to which he may refer. This is to be regarded as an essential feature of any work on recent advances.

The author has fulfilled his stated object very ably, and this book will certainly be of service "to those surgeons who, through lack of time or library facilities, have found research into the welter of modern surgical literature difficult".

### X-RAY EXAMINATION OF THE SKULL, SINUSES AND MASTOIDS.

YET another valuable handbook is to hand of a series published by the Year Book Publishers Incorporated, of Chicago. It is entitled "The Skull, Sinuses and Mastoids", by Barton R. Young, Professor of Radiology, Temple University Medical School.[2] The author describes and illustrates the X-ray appearances of this region at various stages of development with the variations occurring in diseased conditions. The book is arranged in atlas form, with illustrations on the right hand page and descriptive text on the left. The illustrations are of the highest quality and the text is sufficiently extensive to describe them.

All films of anterior and posterior sinuses are taken in the upright position, while those of the temporay areas and mastoids are taken in the horizontal position. The Potter-Bucky diaphragm is used at a distance of four feet in most cases, but in the mastoid areas, the use of plain films without the Potter-Bucky diaphragm is thought to give greater detail.

Steroscopic lateral, postero-anterior and antero-posterior films are used as a routine, but these are supplemented by additional views when the clinical findings suggest that they may be of use. The author stresses the importance of a full knowledge of the clinical findings before proceeding to interpretation. The section on the infant skull is well covered with excellent illustrations of abnormal conditions, such as

[1] "Recent Advances in Surgery", by Harold C. Edwards, C.B.E., M.S., F.R.C.S.; Third Edition; 1948. London: J. and A. Churchill, Limited. 8" × 5¼", pp. 448, with many illustrations. Price: 24s.

[2] "The Skull Sinuses and Mastoids: A Handbook of Roentgen Diagnosis", by Barton R. Young, M.D.; 1948. Chicago: The Year Book Publishers Incorporated. 5¼" × 8", pp. 334. Price: $6.50.

craniostenosis, Albers-Schönberg disease, *osteogenesis imperfecta*, chondrodystrophies *et cetera*.

The author recommends that suspected skull fractures should be examined after shock has passed off, unless a depressed fracture is possible. It is also pointed out that some skull fractures may be missed even with the most careful technique. It is often very difficult to distinguish between vascular lines and sutural markings, but generally the fracture line is more sharply defined.

The appearances in the presence of skull tumours both primary and secondary are very well illustrated. The author points out that increased convolutional markings suggest intracranial pressure, but are by no means diagnostic. He only touches on encephalography incidentally, as this type of work is really outside the scope of the handbook.

The most informative section of this work is that on mastoid diseases. The use of a Bullitt apparatus for fixation of the head allows repetition pictures to be made always with the same projection on the film. However, all possible projections of the mastoid, such as Laws and Stenver's position together with tangential views, are described.

The various pathological conditions are described in good detail and excellently illustrated. This handy work can be recommended to all radiologists as being up to date and comprehensive.

## DISEASES AFFECTING THE VULVA.

THE third edition of "Diseases Affecting the Vulva" by Elizabeth Hunt has recently been published.[1] In general the book is very similar to the previous edition. There is one new colour plate, illustrating telangiectasis and *lichen simplex* of the labia, and a descriptive section on telangiectasis has been added. It is to be regretted that there is no improvement in the clarity and detail of the thirty-six photomicrographs presented.

Attention has been drawn to inflammation of the vulval skin due to mechanical causes, which may result from the use of ill-fitting corsets or the lack of proper abdominal support. In a consideration of ulcers of the vulva, ulcers due to anaerobic streptococci and to underlying bone disease have been included, and reference is made to the association of diseases of the eye and skin with acute recurrent ulcers in the mouth and on the genitalia. Other additions include recent advances in therapy, such as the use of sulphonamides and penicillin for microbic affections of the skin and of penicillin for gonorrhœa and syphilis. Good results are claimed for vitamin therapy, vitamin *B* being prescribed for leucodermia, large doses of vitamin *A* for *lichen planus* and *lichen simplex*, and vitamin *D* for *lupus vulgaris*.

Attention is drawn to the possibility of the causation of dermatitis by benzocaine and procaine and to drug eruptions due to sulphonamides and stilbœstrol. "Benadryl" is included in the treatment for urticaria and ultra-violet light is said to be of value in psoriasis and monilial conditions. Good results have been obtained with a solution of sodium bicarbonate mixed with glycerin in cases of *lichen planus*.

Many gynæcologists will not be prepared to accept the identification of *lichen sclerosus* with *leucoplakia vulvæ*. Neither will they agree with the use of the electrocautery or diathermy for carcinoma of the vulva. There is no mention of the use of anti-coagulants for thrombophlebitis, and diathermy is the only treatment suggested for cure of urethral caruncle. In the section on vaginal and intestinal organisms the possibility of trichomonas infection via the bowel is not mentioned; neither are the many and varied recognized forms of treatment for trichomoniasis. A valuable form of treatment for monilial infections, namely, painting the vulva and vagina with 1% aqueous solution of gentian violet, appeared in the last edition, but has been omitted from the present one. In the treatment of *herpes zoster* no mention is made of the value of pituitrin or of vitamin *B*.

The chapter on venereal diseases would have been better omitted and reference made to a gynæcological text-book.

The book is of value in that it draws attention to the fact that the vulva is part of the integument of the body rather than a genital organ. However, as part of the genital tract it is subject to hormonal influences not seen in the skin of other parts of the body, and for this reason the lesions are somewhat different. It is regrettable that this fact was not stressed by the author.

[1] "Diseases Affecting the Vulva", by Elizabeth Hunt, B.A., M.D., Ch.B. (Liverpool); Third Edition; 1948. London: Henry Kimpton. 9½" × 6", pp. 212, with many illustrations, some of them coloured. Price: 25s.

# Books Received.

*[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]*

"Clinical Laboratory Methods and Diagnosis", Volumes I and II, by R. B. H. Gradwohl, M.D., D.Sc., F.R.S.T.M. and H. (London), pp. 3742; Volume III, "Parasitology and Tropical Medicine", by R. B. H. Gradwohl, M.D., D.Sc., F.R.S.T.M. and H. (London), and Dr. Pedro Kouri, pp. 876. Fourth Edition; 1948, with illustrations. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 6¾". Price: £15.

A three-volume text-book of laboratory procedures with their interpretation.

"Zinsser's Textbook of Bacteriology", revised by David T. Smith, M.D., Donald S. Martin, M.D., M.P.H., Norman F. Conant, Ph.D., Joseph W. Beard, M.D., Grant Taylor, M.D., Henry I. Kohn, Ph.D., M.D., and Mary A. Poston, M.A.; Ninth Edition; 1948. New York: Appleton-Century-Crofts Incorporated. 9½" × 6½", pp. 1044, with illustrations. Price: $10.00.

The application of bacteriology and immunology to the diagnosis, specific therapy and prevention of infectious diseases, for students and practitioners of medicine and public health.

"A Treatise on Hygiene and Public Health: With Special Reference to the Tropics", by Birendra Nath Ghosh, M.B.E., F.R.F.P. and S. (Glasgow), F.R.S. (Edinburgh); Twelfth Edition; 1948. Calcutta: Scientific Publishing Company. 8½" × 5", pp. 784, with illustrations. Price: 15s.

The twelfth edition since 1912.

"Nursing for the Future: A Report Prepared for the National Nursing Council", by Esther Lucile Brown, Ph.D.; 1948. New York: Russell Sage Foundation. 9" × 6", pp. 304. Price: $2.00.

A study in the education of nurses.

"The Surgery of the Stomach and Duodenum", by T. H. Somervell, M.A., M.B., B.Ch. (Cantab.), F.R.C.S. (England); 1948. London: Edward Arnold and Company. 9" × 5½", pp. 558, with illustrations. Price: 45s.

A handbook for the practising surgeon based on extensive experience, observation and reading.

"Emergencies in Medical Practice", edited by C. Allan Birch, M.D., F.R.C.P.; 1948. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5½", pp. 482, with illustrations. Price: 25s.

Information for the practitioner or hospital physician faced with an acutely ill patient or a critical situation.

"Everyday Problems of the School Child", by Agatha H. Bowley, Ph.D.; 1948. Edinburgh: E. and S. Livingstone, Limited. 7" × 4½", pp. 158, with illustrations. Price: 7s. 6d.

Advice to teachers by a psychologist.

"Philosophy of Literature", by Gustav E. Mueller; 1948. New York: Philosophical Library. 8½" × 5½", pp. 244. Price: $3.50.

Undertakes to demonstrate "how the evaluative world view, which dominates and distinguishes races, ages and cultures, rendering them intelligible, also directs their imagination, manifest in the art of the word".

"Handbook of Orthopædic Surgery", by Alfred Rives Shands, Jr., B.A., M.D., in collaboration with Richard Beverly Raney, B.A., M.D., illustrated by Jack Bonacker Wilson; Third Edition; 1948. St. Louis: The C. V. Mosby Company. 8½" × 5½", pp. 597, with illustrations.

For the medical student and the general practitioner.

"The Modern Management of Gastric and Duodenal Ulcer", edited by F. Croxon Deller, M.D., M.R.C.P.; 1948. Edinburgh: E. and S. Livingstone, Limited. 9" × 6", pp. 230, with illustrations. Price: 20s.

An essentially practical book based on experience.

"Philosophy in Wit", by Emil Froeschels; 1948. New York: Philosophical Library. 8½" × 5½", pp. 84. Price: $2.75.

An investigation into the nature of wit by the former professor of medical philosophy at the University of Vienna.

"Pharmacopœia of Proprietary Drugs, 1948", by H. D. Jackson, M.M., M.P.S., Ph.C.; 1948. Sydney: Grahame Book Company. 7" × 4¾", pp. 61.

An alphabetical list of proprietary drugs with their use and dose and details of packing.

"A Synopsis of Regional Anatomy", by T. B. Johnston, C.B.E., M.D.; Sixth Edition; 1948. London: J. and A. Churchill, Limited. 8" × 5", pp. 448, with illustrations. Price: 18s.

A new edition of a book intended essentially for revision purposes after dissection has been completed.

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## NAMES.

JULIET'S famous postulate regarding the absence of correlation between nomenclature and essential characteristics, as exemplified in the olfactory-stimulating properties of members of the genus *Rosa*, received ready assent from Romeo, but like most generalizations it is only a part truth. For names and objects named react upon one another and mostly attain a state of equilibrium in which they have a common value. In Capulet's garden, of course, this equilibrium was profoundly disturbed; to be Juliet, and a Capulet, or Romeo, and a Montague, was nothing beside being a lover—that is, from the lovers' point of view; but for Juliet's kinsmen the name of Montague determined their assessment of Romeo and merited for him death. At the risk of making another generalization it may be said that names when first bestowed usually have an intrinsic value and significance and may profoundly affect the thing named; later they take on more and more the character of their bearer. When the young mother names her baby after the kind and/or handsome young doctor at the maternity hospital (or after her favourite film star) the name seems to carry virtue in itself, and rather vaguely she hopes that the child will benefit; later, if the child shows reluctance to assume this virtue, the mere mention of the same name may revolt some long-suffering school teacher or neighbour. On the other hand, the disciples were first called Christians at Antioch, apparently in derision by their foes, and yet in a few years men and women died for the honour of carrying the name. An exile in a new land soothes his nostalgia by importing the names of home places of pleasant memory; yet to a native Australian such a name as Surry Hills may well have a completely different significance. The names of political parties, their import and their public appeal form an illuminating study; topical comment is not perhaps appropriate here, but we may refer to Hilaire Belloc's "But Soft: We Are Observed!" in which we find that in 1979 the parliaments of the Great Powers had

> two sober parties, Communist on the right and Anarchist on the left, who between them maintained the Majestic Rotation of Representative Government, and against Annihilationism they fought for their lives.

It is profitable at times to reflect on the names of diseases and to realize that the patient or the relatives may be much less impressed by the smell of the rose than by the name. The mother who is told airily that little Jimmy has "a touch of bronchitis" may not be reassured into appreciating that the patient does not look very ill and is not very ill; her horrified mind may be dwelling on Uncle Henry, who was said to have "bronchitis" and who ended his days in a distressing state of dyspnœic invalidism. Names such as malignant tertian malaria and pernicious anæmia may have long since lost their menace to the doctor, but they can terrify the patient; such violent names, now rendered almost meaningless by modern therapy, would be better abandoned. The increasing use of the name poliomyelitis instead of infantile paralysis must surely be helpful in allaying parents' fears that every victim of the virus will be seriously paralysed. Patients and relatives are often not happy until a label is given to an illness—indeed their cooperation in treatment may depend on this—but the fact only helps to recall how inadequate such names may really be as indications of essential ætiology or underlying pathology. Who has not been asked if a patient is suffering from "dropsy" and felt a little bewildered at the satisfaction given by a definite answer when his own mind is revolving over the many causes of œdema? Euphemisms may or may not be commendable. It is only sometimes right for a patient to be ignorant of his true state, but some names carry a degree of horror in themselves; cancer can be a very cruel word to use lightly, when many other words will convey the same meaning and yet cause less shock. Polite terms, such as social disease, spot on the lung, nerve trouble, are often mere genteelisms, but they will be right for some patients, just as more homely and colloquial terms will be right for others. The rule runs parallel with Eugene Field's lines:

> Father calls me William, sister calls me Will,
> Mother calls me Willie, but the fellers call me Bill!

Investigation of the origin of medical names brings much information and many surprises. We still use the term malaria, though we no longer fear the unhealthy exhalations of swamps, and Mussolini broke an important link in this word's history when he drained the Pontine marshes. An artery seems likely to continue to be known as such, though the word is said to mean "air-conveyor" and no one has held the corresponding view of the circulation for centuries. Glaucoma means a grey-green tumour and is, according to a recent annotation,[1] "a useful word, because being meaningless it serves to cover our uncertainty as to the pathology of the disease". In the same annotation the writer refers to the suggestion that a cataract was so named from the ancient theory that it was caused by a fall of inspissated material into the pupil, but he favours the second meaning of *cataracta*—a portcullis—as the significant one, and it is certainly appropriate to this barrier in the eye's gateway. This writer also questions the terms hypermetropia and myopia, interpreting them to mean respectively "an eye beyond measure", which would be inappropriate for an eye that is usually too small, and "a closed, and therefore by inference a small eye", which does not describe the usually oversized "myopic" eye. However, Sir Stewart Duke-Elder in "The Practice of Refraction" supports the term hypermetropia,

[1] *The British Journal of Ophthalmology*, July, 1948.

which was suggested by Donders in 1858, as against hyperopia which Helmholtz suggested in the following year, and explains the "closed eye" of myopia as referring to the habit which short-sighted people frequently have of half-closing the lids when looking at distant objects so that they may gain the advantage of a stenopœic opening. There has been a good deal of discussion about the naming of syphilis. Indeed it had many names, for example, the French disease, the Neapolitan disease, the Polish disease *et cetera*—graceful tributes all from some neighbouring country—but Fracastoro seems to have given it a permanent designation by inventing the name Syphilos for the swineherd hero of his poem on the disease which was published in 1530. Cæsarean section is popularly regarded as the mode of birth of Julius Cæsar, but H. W. Haggard in "Devils, Drugs and Doctors" points out that Cæsar's mother lived for several years after his birth and the operation was not then performed on living women. He explains the name from the fact that the Roman law required this procedure in case of the mother's death; the laws under the emperors became Cæsarean laws and the operation the Cæsarean operation, and so it has remained. Vitamins, first called "vitamines" by Funk in 1912, were later recognized as not being amines, and the final "e" was dropped by general consent in 1920; but the name remains as a tribute to their vital qualities with a meaningless last syllable for good measure. So we might go on quoting names whose original meaning has been lost, but which have taken on a new meaning.

It is very debatable that the trend in anatomical nomenclature towards replacing historical names with descriptive terms is justified. Does *tuba auditiva* or *tuba pharyngotympanica* serve better than Eustachian tube, *confluens sinuum* than *torcular Herophili*, *tendo calcaneus* than *tendo Achillis*, or *aquæductus cerebri* or *aquæductus mesencephali* than aqueduct of Sylvius? May not the dry bones of anatomy gain by being clothed at least in part with the rich garments of history? The bacteriologists seem to value historical associations in their much younger science and we find terms being introduced such as Pasteurella, Escherichia, Klebsiella, Shigella and Neisseria, commemorating giants of bacteriology. It is pleasing that *Rickettsia burneti* is now accepted as a standard name, particularly as it was suggested by E. H. Derrick, who had himself carried out notable work in the related field, but was prepared to let posterity honour his colleague F. M. Burnet. It must be admitted that the naming of a disease from the first person to describe it opens up difficulties and rival claims, especially when the investigator attaches his own name. The problem is not always solved by linking together individual investigators, as in Hand-Schüller-Christian's disease, Besnier-Boeck-Schaumann's syndrome or Klebs-Löffler bacillus, especially if mutual acknowledgement is lacking. But this is a thorny problem. We seem to have quoted here many names whose intrinsic meaning has gone out of sight and to have either accepted or advocated their continued use. It seems right, however, to urge the claims of fitness and literary quality on those who coin new names. It is a pity, for example, that many names derived from digitalis ignore the fact that the essential part of the word is "digit"; a name which takes over less than that has no real meaning and loses the charm associated with the foxglove or "ladies' fingers" of a former day. Caustic comment has been made recently[1] on the introduction of "silly names" for penicillin products which appear to have neither scientific merit nor literary quality. Names should at least not offend the ear, for, as Carlyle says, giving a name is a poetic art; and it is right that they should have sound meaning and not be as women's names which, Ernest Rhys tells us,

> keep murmuring like the wind
> The hidden things that none for ever tells.

# Current Comment.

## FATTY LIVER DISEASE IN INFANTS.

FATTY LIVER DISEASE in infants in the British West Indies is the subject of an interesting study by J. C. Waterlow in a special report of the Medical Research Council.[2] In the report attention is directed toward the notorious complexity of diseases due to malnutrition, the syndromes of which, though similar in essential features, are modified by racial, geographic and seasonal features. Malignant malnutrition and infantile pellagra are examples of syndromes which are common throughout the tropical world and have as their fundamental features œdema, muscular wasting and fat accumulation in the liver. In some parts of the world lesions of skin and mucous membranes figure so prominently that the name "Kwashiorkor", meaning "red boy" in a Gold Coast dialect, is given to the disease. In spite of predominant pellagroid features it is generally agreed that vitamin therapy is not curative, though it may reduce the superficial lesions. Waterlow maintains that the condition he describes is a distinct entity, the basis for the essential features of which is as yet obscure, and he emphasizes that it is more than the mere sum of several well-known deficiency states. In support of this view are the high mortality, the lack of response to vitamins and most foodstuffs rich in protective factors, and the constant presence of fat accumulation in the liver. He estimates that there are, in a population of one and a quarter million in the British West Indies, several hundred cases each year. The disease affects young children in the first two years of life, especially after the termination of breast feeding. The average age of the infants when first examined was ten and a half months. The presenting features were œdema and vomiting, occasionally diarrhœa, and examination revealed an enlarged liver and muscular wasting. It was thought that the œdema was related to the reduction in the amount of serum albumin and to a total serum protein level in the vicinity of 4·5 grammes per 100 millilitres. No relation, however, was defined between the severity of œdema and the extent of the reduction of the amount of serum protein, an observation which led to speculation upon the theory that hypoproteinæmia was the sole cause of œdema. In these cases the need for a moderate caloric intake to maintain life during the development of hypoproteinæmia is emphasized and, as the Calories taken are derived from carbohydrate with its recognized faculty for promoting water storage, this circumstance may have contributed to the œdema. The hypoproteinæmia was part of a general depletion of body protein from which the liver and muscles did not escape. The loss of weight in the infants with fatty liver disease was less pronounced than in a control group which consisted of those with a subnormal but not necessarily a qualitatively defective diet. A further difference was that in the group with fatty liver disease the quantity of liver fat was much increased above the level of the group with under-nutrition. The results of liver function tests were disappointing, leading once more to the conclusion that the tests designed to estimate one

[1] *The Journal of the American Medical Association*, July 17, 1948, page 1043.

[2] "Fatty Liver Disease in Infants in the British West Indies", by J. C. Waterlow; 1948. Medical Research Council of the Privy Council, Special Report Series Number 263. London: His Majesty's Stationery Office. 9½" × 6", pp. 96, with illustrations. Price: 2s.

aspect of liver function can only detect severe damage. The absence of jaundice or of significant increase in the level of serum bilirubin, the slight increase in the level of serum alkaline phosphatase, and the negative result attending the colloidal gold test all bear witness to the lack of help in diagnosis afforded by these tests in fatty liver disease. Bromsulphthalein clearance was impaired only when liver damage was of sufficient severity to endanger life. Liver biopsy was of value in confirming the diagnosis of fatty liver and in following the course of recovery.

The outstanding feature of the disease is, of course, the fat accumulation in the liver, and still more remarkable is its failure to respond to methionine and choline, the usual lipotrophic substances, the lack of which produces gross fat accumulation in the liver in laboratory animals. Chemical poisons and infectious hepatitis have been carefully excluded in these cases. It is pointed out that the fat accumulation is not specific of the disease, because fat accumulation is a feature of many conditions, including those due to chemical poisons, infections and starvation; and it is also emphasized that the problem of fat in the liver is highly complex. In starvation and after injections of pituitary extract fat in the liver comes from the depots and in choline deficiency from the food. In choline deficiency therefore the caloric intake bears a direct relationship to the quantity of fat in the liver. Animals in an active growth phase may use their essential amino acids for building body tissue, so that a relative deficiency is produced, and methionine-supplied methyl groups for the synthesis of choline are unavailable for this purpose. Waterlow considers that this particular fatty liver disease of infants differs from the bulk of human fatty liver disease in that the source of fat is exogenous, a point supported by the relatively high caloric intake on a background of an otherwise deficient diet. This high carbohydrate accompanied by low protein intake is also important in the determination of œdema. The failure to respond to very large doses of methionine or choline is difficult to explain, but the response to milk suggests that, although lipotrophic activity of casein is related to its methionine content, there is a possibility of an active factor other than methionine. Waterlow, however, does not favour the view that fatty liver disease is a deficiency of some substance yet unknown, but lays emphasis on three factors, namely, the metabolic demands of the growing organism, prolonged depletion of protein, and carbohydrate overloading. Protein deficiency may, by virtue of the loss of certain labile components of enzyme systems intimately associated with fat metabolism, accelerate a fat accumulation which will remain unaffected by the lipotrophic components of the protein.

## AN ARTIFICIAL HEART.

IT would be decided understatement to say that cardiac surgery is complicated by the presence of blood in the heart and great vessels. A good deal of ingenuity has been displayed in the attempt to provide a bloodless field, but the results have been physiologically inadequate. The most promising device so far is a cardio-pulmonary machine recently described by V. O. Björk of Stockholm.[1] This machine, constructed by Crafoord and Andersson, is designed to maintain an adequate blood-flow through the brain, following Crafoord's finding in 1935 that it was possible to suspend the flow of blood to all organs but the brain for a considerable time without damaging them. Björk states that he has clamped both superior and inferior *venæ cavæ* of a dog for thirty-three minutes, rendering the heart bloodless but maintaining the blood-flow to the brain alone with the cardio-pulmonary machine; the dog survived with no sign of organic damage and became father to eleven puppies. The method of oxygenation is by spinning a row of plates which dip into a trough of blood and so expose constantly changing thin films of red cells to oxygen. This is a real advance though there are still deficiencies in the machine, particularly in relation to the breakdown of red cells. We are still, as *The Lancet* points out, a long way from the goal of being able to isolate the human heart from the circulation during intracardiac surgery, and other methods of approach are being devised. However, the rapid progress of cardiac surgery should be a strong stimulus towards the overcoming of technical difficulties.

[1] *The Lancet*, September 25, 1948.

## INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM IN MUMPS.

IT is well known that the central nervous system is not infrequently involved in mumps. Though not a serious disease in the sense that it carries a risk to life, mumps causes a considerable degree of disability during its florid period, and is a most unwelcome visitant of military camps and other places where susceptible young people are closely gathered together. Apart from the unfortunate sequels of epididymo-orchitis, no untoward effects are seen as a rule after an attack, even in an adult. The assault on the nervous system which may at times be somewhat alarming for a time, rarely leaves an aftermath. Serious sequels have been reported, however, and even death, so that the onset of headache, drowsiness and neck stiffness cannot be regarded lightly. The frequency of nervous complications has aroused a good deal of interest from time to time, and in some of the epidemics which have been studied from this point of view the incidence has been considerable, exceeding 20%. An analysis has been published by J. W. Brown, H. B. Kirkland and G. E. Hein of an outbreak observed in young American men, chiefly soldiers, in England during the recent war.[1] Lumbar puncture was performed on 77 consecutive patients, and the cerebro-spinal fluid studied. The tests performed were cell counts, estimation of the globulin, sugar and chlorides, and in over half the number qualitative estimation of the protein also. The time chosen for the test was between the eighth and twelfth days, unless the appearance of nervous signs made earlier examination necessary. Nine of the patients showed signs of meningo-encephalitis, but eighteen of the remainder had increased cell counts in the spinal fluid. It was observed that in the latter group epididymo-orchitis was also present in 42%. This is not surprising, for metastatic manifestations of mumps not infrequently are multiple in the same patient. No correlation was observed between the degree of pleocytosis and the clinical evidences of involvement of the nervous system. Further, increased cell counts were found in a number of patients who showed no signs whatever of nervous complications. Increase in the amount of protein in the spinal fluid was not great; it exceeded 50 milligrammes *per centum* only once, though lesser increases were found in some patients who had no other sign of cerebral or meningeal involvement. No abnormal findings were observed in the content of sugar or chlorides.

The clinical evidences of meningo-encephalitis included headache, stiffness of the neck, nausea, vomiting and vertigo. Except in one instance these were not severe and were promptly relieved by lumbar puncture. It is perhaps curious that even in this small series no mention is made of drowsiness. The single patient who was severely affected apparently had mumps; he had bilateral epididymo-orchitis and meningo-encephalitis, but no demonstrable parotitis. He suffered from confusion, tremor of the arms and head, and some cranial nerve palsies, and had residuals of ataxia and vertigo and affective mental changes, all of which have not completely disappeared even after over three years. The authors discuss the cause and significance of meningo-encephalitis as a feature of attacks of mumps, and believe that it is probable that every patient suffering from this disease is subject to the known neurotropic effects of the virus. The interest of their observation lies in their demonstration of the frequency of involvement of the meninges and possibly also to some unascertained degree the nervous tissue, even though such affections seem to be mild as a rule. It would appear that the old problem of encephalitis accompanying infectious disease still merits study.

[1] *The American Journal of the Medical Sciences*, April, 1948.

# Abstracts from Medical Literature.

## PATHOLOGY.

### Cicatrizing Enteritis (Regional Ileitis).

SHIELDS WARREN AND SHELDON C. SOMMERS (*The American Journal of Pathology*, May, 1948) have analysed one hundred and twenty unselected cases of cicatrizing enteritis (regional ileitis) and have prepared a comprehensive review of the literature on the acute, subacute and chronic stages of the disease. They state that the terminal part of the ileum of a young adult is most often affected, in either sex and in members of any race, but the jejunum, upper part of the ileum, appendix, caecum or colon may be involved. The ætiology is unknown. The characteristic gross findings are sharply demarcated induration and œdema of intestine and its mesentery, with enlargement of regional lymph nodes. Microscopic sequences indicate that swelling and proliferation of lymphatic endothelium in intestine and lymph nodes cause occlusion of lymphatics and resulting œdema. Granulomata containing giant cells are formed by these cells throughout the intestinal wall and in mesentery, lymph nodes and liver. These granulomata slowly hyalinize, usually without necrosis, or are obscured by secondary bacterial infection. In late stages, subacute and chronic inflammation, fibrosis and muscular hypertrophy of the intestine are prominent. The authors consider that cicatrizing enteritis (regional ileitis) is an acceptable pathological entity.

### Persistent "Insect Bites".

ARTHUR C. ALLEN (*The American Journal of Pathology*, March, 1948) has made a histological study of the reactions to the "bites" of ticks, chiggers, mosquitoes, and unidentified arthropods. He states that the reaction, which consists of a dense dermal infiltrate characterized by large numbers of eosinophilic leucocytes, plasma cells, and histiocytes, may be mistaken for Hodgkin's disease, *mycosis fungoides*, atypical lymphoblastoma, histiocytosis, and the heterogeneous group of "eosinophilic granulomata". The lesion is often associated with a pseudoepitheliomatous hyperplasia which may be confused with squamous-cell carcinoma. The association with an eosinophilic dermal infiltrate and with epidermal inclusion cysts provides helpful differential clues. With one exception, no basic difference was noted in the histological reaction of the skin to the various arthropods studied. The striking exception is the almost complete absence of eosinophilic leucocytes in the eschar or primary lesion of scrub typhus caused by the larval mite (*Trombicula akamushi* and related species). It is emphasized that the reaction to the "bites" of arthropods may persist for many months and that, in general, no appreciable difference is noted in the histological reaction in lesions lasting from three weeks to two years. It is therefore concluded that the stimulating agent of the arthropod somehow must persist actively in the focus of these lesions for a remarkably long time. A single cutaneous lesion with the histological picture suggestive of Hodgkin's disease or other lymphoblastoma should always be suspected as having been caused by the bite of an arthropod until conclusively proved otherwise. The history of an insect bite may not be volunteered after a lapse of many months. The cutaneous reactions of individuals, even of the same race, to different arthropods vary not only in the acute stage, but also in the persistence, degree and quality of the histological reaction. It remains to be determined precisely what agent in the venom or embedded parts of the arthropod, or both, is responsible for the cutaneous reaction.

### Allergic Hyperglobulinosis and Hyalinosis (Paramyloidosis).

GUNNAR TEILUM (*The American Journal of Pathology*, March, 1948) states that, as a feature common to Boeck's sarcoid and a number of other pathological conditions associated with hyperglobulinæmia, the reticulo-endothelial system is found to contain precipitates of homogeneous substance passing on to hyalinosis (paramyloidosis). The alterations with regard to pathogenesis, structure, and phasic development (proliferation of reticulum cells and precipitation), localization, and alterations of the blood (hyperglobulinæmia) must be considered analogous to atypical and experimental amyloidosis. The common primary basis is supposed to be an allergic hyperglobulinosis in the reticulo-endothelial system, determined by persistent or repeated stimulation of immune mechanisms. In Boeck's sarcoid the following points, among others, are thus explained: (i) the localization in the reticulo-endothelial system; (ii) the morphological features (epithelioid-cell granulomata without any tendency to necrosis; the occurrence of "extragranulomatous" precipitates; the paramyloid phase with frequently concentric, hyaline rings in the border zone; the development of a periarterial hyaline zone in the spleen and in other organs, analogous to the periarterial fibrosis of the spleen in *lupus erythematosus disseminatus*); (iii) the occurrence of hyperglobulinæmia, which is a useful diagnostic sign in Boeck's sarcoid; (iv) the state of immunity, in accordance with the generally accepted view of Boeck's sarcoid as a condition with a high immunity (positive anergy). Like the different antibodies, various forms of hyalin and paramyloid must also, after these findings, be considered products of plasma cells and other reticulo-endothelial cells.

### Some Aspects of the Evolution of Silicotic Lesions.

I. COSTERO (*The American Journal of Pathology*, January, 1948), after studying the structure and evolution of the silicotic node with the silver impregnation methods of Rio-Hortega, has reached the following conclusions. The histological basis of all lesions induced in the human lung by siliceous dust is the proliferation of the reticular fibres. After proliferation these fibres are partially or wholly transformed into collagen and undergo hyalinization and retraction. The silicotic node continues its growth as long as there are reticular fibres left; growth is arrested when collagenization is complete. The reticular fibres of the nodule originate mainly in the adventitial layer of small vessels, especially the venules which have been attacked by siliceous dust deposited in their adventitial lymphatic spaces. Fibrogenesis from regional histocytes is of secondary importance. The nodules grow by (*a*) apposition of adjacent nodules in the later stages of development, (*b*) organization of the exudate of the desquamative pneumonia which marks the limit of the developing nodules, and (*c*) transformation of adjoining atelectatic zones. The adventitial lymphatic space of the blood vessels is frequently found dilated and obstructed by proliferating reticular fibres. Sometimes the nodes are penetrated by newly formed capillaries arising from nearby interalveolar septa. Many of the silicotic nodules undergo a softening process due to the penetration of newly formed capillaries and to the autolytic action of macrophages. In the softening foci the author has found chrysophilic masses and basophilic crystals whose origin and significance cannot be interpreted at present. The macrophages found in silicotic lesions are first seen around the vessels, shortly after the beginning of the proliferation of reticular fibres. They contain great amounts of detritus and siliceous particles. They are destroyed later when they are compressed by bundles of hyalinizing collagen and also in great part by autolysis. The elastic fibres disappear in the completely constituted lesions. Their disposition outside the latter is indicative of the traction originated by the shrinking of silicotic nodules in the stage of collagenous transformation. Besides the typical silicotic nodule there also appear diffuse sclerotic plaques, peribronchial sclerosis, and proliferative pleuritis. These three lesions have special characteristics which can be related to the different types of lymphatic drainage pertaining to each region; however, this histogenesis, structure and evolution are similar to those of the typical silicotic nodule.

## MORPHOLOGY.

### Bowman's Capsule in Kidney.

E. MAYER AND L. A. OTTOLENGHI (*The Anatomical Record*, December, 1947) report the study of the structure of Bowman's capsule in the kidneys of dogs and cats. The epithelial lining of Bowman's capsule in the kidneys of mammals varies from very shallow endothelium-like cells to cuboidal cells, depending on age, species and the stimuli to which the individual kidney has been exposed. Under certain abnormal conditions the capsular epithelium proliferates so that several layers of squamous cells are produced—the so-called epithelial crescents in human pathology. While these structures are well known, little attention has been given to the occurrence of tubular epithelium in the space of Bowman's capsule. These epithelial formations are continuous with the proximal convoluted tubule, but are distinct from the cells which line the capsule. Protruded tubular epithelium occurring in the space of Bowman's capsule is, therefore, distinct from variations of capsular epithelium such as "cuboidal cells" or nephritic "crescents". The protruded epithelium

is continuous with the proximal convoluted tubule, has the same type of nuclei, and, probably, has a similar metabolism. It is likely that nephrons with protrusions maintain their function. Protrusions are found in control dogs as well as in animals which have been subject to various drug experiments. There was no correlation between the occurrence of protrusions and the race, sex, age or history of the 58 dogs examined. The phenomenon is seen in mature corpuscles only of both young and adult dogs. Observations in cats showed protrusions similar to those in dogs. There are two different ways in which protrusions can form, namely, by invagination or by telescoping. The forces which push the tubular epithelium into the capsular space are unknown. Factors which act violently, or within a short time (agonal struggle, histological procedures *et cetera*), are ruled out on the basis of several observations. Slow variations in intrarenal pressure during life are more likely to play a role in the production of protrusions.

### Development of Cervical Vesicles in Man.

F. D. GARRETT (*The Anatomical Record*, January, 1948) draws attention to the fact that the group of ectodermally lined cavities in the neck region usually collectively referred to as "cervical sinus" consist (on each side) of two independent and ultimately closed vesicles, one derived by evagination from the lining of the second branchial cleft and one resulting from transformation of the fourth branchial cleft. In addition it is the cervical sinus proper or precervical sinus which becomes almost completely separated into a rostral portion associated for a time with the second cleft and a caudal portion associated with the third and fourth clefts. The precervical sinus disappears relatively early without being cut off from the surface as a closed vesicle. The second and fourth clefts, left by the obliteration of the precervical sinus as independent closed vesicles lying in close relationship to the glosso-pharyngeal and vagus nerves respectively, undergo regression and disappear, the second rather promptly, the fourth after a short period of expansion. The fourth vesicle (remains of fourth cleft), at first lying in intimate contact with the thymus-parathyreoid III complex, shows progressive withdrawal from that contact during the period of its regression. There is no indication of a contribution to the thymus of cells from the fourth vesicle.

### Histology of Neuro-Hypophysis.

J. D. GREEN (*The Anatomical Record*, March, 1948) has studied the histological structure of the median eminence and of the neural stalk in man with special reference to the blood vessels and nerve fibres which they contain. The sheaths of the hypophysio-portal vessels consist of ordinary connective tissue in which smooth muscle cells, collagen and reticular fibres may be recognized. The structure of the vessels indicates that the direction of blood flow in the hypophysio-portal system is from above downward. This is confirmed in observations on rats. Nerve endings are described within the connective tissue sheaths and in the *pars tuberalis*. Certain histological differences between the median eminence and neural stalk on the one hand and the neural lobe on the other are emphasized. A neuro-vascular zone which does not appear to have been described previously is reported and discussed briefly.

### Anomalous Urinary Bladder.

M. TROTTER AND J. C. FINERTY (*The Anatomical Record*, February, 1948) describe in a Negro male, aged eighty-five years, a urinary bladder which is divided into two chambers of approximately equal capacity by a thick septum (more than twice the thickness of the bladder wall). The septum lies in an oblique plane approximately halfway between the frontal and sagittal planes. The superior chamber lies to the right of the midline and somewhat posterior to the inferior chamber, and the walls of each are of approximately equal thickness. These chambers communicate by means of a circular orifice in the septum. The ureters terminate in the inferior chamber, with the right ureter traversing the septum. The characteristics of this specimen support its classification as a congenital hour-glass bladder.

### Renewal of Intestinal Epithelium.

C. P. LEBLOND AND C. E. STEVENS (*The Anatomical Record*, March, 1948) describe their attempt to discover the fate of the unusually large number of cells undergoing mitosis in the crypts of Lieberkühn in the duodenum and ileum. It was first postulated that, in order to maintain the steady state of the tissues, there should be a loss of cells balancing the production of newly formed cells. Since histological signs of a cell loss are visible only at the tip of the villi, it is concluded that the cells formed in the crypts of Lieberkühn move upward along the side of the villi to be ejected when they reach the tips of the villi. The authors state that it is sometimes possible, especially in starved rats, to visualize the extruded cells in the intestinal lumen. The magnitude and speed of this phenomenon were assessed. The epithelial cells were found to live 1·57 days in the duodenum and 1·35 days in the ileum. As these values also refer to the time taken by the cell to move from the crypt to the villi tip, they express the "turnover time" of the whole intestinal epithelium.

### Vestigial Cardiac Structures.

R. WRIGHT, B. J. ANSON AND H. C. CLEVELAND (*The Anatomical Record*, March, 1948) report an investigation of the atrial variations in a large and consecutive series of adult hearts. Records are presented of the size of the *crista terminalis* (443 specimens), of the valve of the inferior *vena cava* (512 specimens), and the valve of the coronary sinus (in 226 hearts). The valve of the inferior *vena cava* and the valve of the coronary sinus are discussed on the basis of size, form and interrelationships. It is apparent that a greater degree of readjustment has occurred in the lateral wall of the right atrium than in the area supero-lateral to the orifice of the inferior *vena cava*, where the crista and the caval valve are likely to remain in close relation with each other. The area of the medial extremity of the valve of the inferior *vena cava* and the limbus of the *fossa ovalis* is close to the interatrial septum, the latter structure being a part of the septum. Readjustment or expansion incident to the attainment of adult morphology has occurred in such a way that, in a larger percentage of cases, the early developmental relationships are retained. Interatrial communications were studied; an anatomical patency was found to be present in 22·9% of cases, a physiological patency in 0·8%. A true Chiari network was found in only one heart of 512 studied. In nine other cases, fibrous cords or strands were found attached to the edge of the caval valve, their other attachment, however, being to the adjoining atrial wall and not to the medial extremity of the *crista terminalis* (as originally described by Chiari). The character of the valve of the *foramen ovale* and the nature and size of the recesses in the atrial septum were recorded for 215 specimens.

### Skeletal Growth after Thyreoidectomy.

H. BECKS *et alii* (*The Anatomical Record*, April, 1948) have made a histological examination of the proximal end of the tibia, the distal end of the third metacarpal, and the ninth and twenty-third caudal vertebræ of rats subjected to thyreoidectomy at birth. This study confirmed the concept obtained from measurements and X-ray examination that skeletal growth and differentiation were greatly retarded but not completely checked. This was shown to advantage in the tibia. Study of the metacarpal was instructive in that closure of the epiphysis of the thyreoidectomized animal did not occur at the normal time, but was delayed beyond the limits of age studied (one hundred and forty-one days). The caudal vertebræ showed great delay in time of appearance of the secondary centres. These centres had not, in fact, appeared in the ninth caudal vertebra at the last age studied, that is, one hundred and forty-one days. The effect of growth hormone on growth and differentiation of these bones was also studied histologically. The concept formulated from X-ray studies, namely, that increase in size occurred without advance in differentiation, was thereby confirmed.

### Tissue Components in Human Female Leg from Birth to Maturity.

E. L. REYNOLDS (*The Anatomical Record*, April, 1948) gives values representing the growth of bone, muscle and the subcutaneous tissues (*plus* skin) which overlie the muscle mass. Measurements were obtained from radiograms of the leg in the female human at seven age levels, namely, birth (30 cases), one month (30), one year (30), 7·5 years (29), 12·5 years (27), 15·5 years (13) and adult (31). Values were taken from antero-posterior radiograms of the calf, at the level of greatest breadth. The data are partially longitudinal. Means are given for the absolute and relative breadths of the tissues at each period, and for the ratios of individual periods to adult size. Total calf breadth, muscle breadth and bone breadth show patterns similar to the general human growth pattern. Fat breadth shows a sharp rise in infancy, a loss in childhood, and another rise in adolescence. The mean breadth of fat in the adult calf is less than the mean breadth at the age of one year. Results are compared with other studies of tissue distribution in man.

# Medical Societies.

## MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held on May 12, 1948, at the Children's Hospital, Carlton, Melbourne, the President, DR. MOSTYN POWELL, in the chair. Part of this report appeared in the issue of October 30, 1948.

### Acute Laryngo-Tracheo-Bronchitis.

DR. NANCY MCNEILL showed a male child, aged three and a half years, who had been admitted to the hospital on April 23 at 10.30 p.m., suffering from acute laryngo-tracheo-bronchitis. His past history was of bronchial colds and fat dyspepsia with associated allergy to the extent of hives, and he had received diphtheria immunization. He had been well recently until two days before admission, when he developed a slight croupy cough with fever and coryzal symptoms, accompanied by steadily progressive difficulty in breathing, which had been diagnosed and treated by his local doctor as asthma, but had shown no improvement. On admission to hospital he was a very sick child in extreme distress, with a temperature of 105° F., a pulse rate of 140 per minute and a respiration rate of 60 per minute. The relevant findings were in his respiratory tract—he had a reddened throat, inspiratory stridor with chest retraction, expiratory wheezing and coarse moist sounds audible all over his chest. He was very restless, but was not cyanosed. Treatment was conservative at first—oxygen, sedation and the steam tent, combined with the administration of penicillin and antidiphtheritic serum. After five hours in the steam tent he showed little change; his colour was still good, but he was, if anything, more restless, so that to the inexperienced eye, it appeared that technical difficulties would make it impossible to perform tracheotomy. The question was decided when he suddenly became cyanosed, and within about five minutes he had stopped breathing; that condition had been present for a minute or two before his trachea could be opened. His colour immediately improved, but there was some trouble in completing the operation as no tube could be found which fitted the trachea satisfactorily, all being too short, and the sucker failed. At that time, after coughing vigorously, he began to develop surgical emphysema of the neck and face. Nevertheless in a few hours he was comfortably back in bed, his colour satisfactory and his tube being cleared in routine fashion with two millilitres of sodium bicarbonate solution half-hourly. On the first day he was fairly drowsy, but well. His heart sounds were loud and clear, but his chest was still full of râles and crepitations. His tube came out and was reinserted, but he gave no cause for anxiety. On his second day, thirty-six hours after tracheotomy, his tube again came out and was replaced, but in the evening it was again dislodged and from that time onwards his condition began to deteriorate. He already had some expiratory wheezing which was improved temporarily by an injection of adrenaline, but after a short time he became cyanosed and it was more difficult to restore his colour. After all had been tried, it became obvious that no tube available was long enough to reach his trachea, so the tracheal dilator had to be held permanently in position. Despite that, his subcutaneous emphysema began to increase, extending on to his trunk, and his condition was far from satisfactory. Dr. Vernon Collins was consulted by telephone and suggested the possibility of mediastinal emphysema in view of the cyanosis, dyspnœa and subcutaneous air. In support of that diagnosis was found loss of normal cardiac dulness and distant heart sounds, though his chest excursion was good. Mediastinal aspiration was attempted, the third and fourth left and right intercostal spaces being tried, but without success. After streptomycin and sulphadiazine had been added to his therapy, the Queen's Memorial Infectious Diseases Hospital was consulted, in the hope that they might have a satisfactory tracheotomy tube; as a result Dr. H. McLorinan himself attended and helped with the case for several hours. He recognized at once the presence of considerable quantities of secretions lower down in the bronchial tree and spent an hour of strenuous work washing and sucking out the thick sticky mucus, using much larger quantities of sodium bicarbonate solution. Yet still he had no tube which was long enough, nor was there any at Fairfield. The child's increasing cyanosis was attributed to œdema of trachea and bronchi, probably with some mediastinal emphysema, and his prognosis seemed hopeless. Over the next few hours he was in terrible and increasing distress, which could not be alleviated by sedation. His condition continued to deteriorate rapidly, with a maximal degree of cyanosis, and he had a pulse rate of over 200 per minute. Local and subcutaneous administration of adrenaline was tried, in the hope of relieving the œdema and any element of spasm, but the emphysema extended over his shoulders and the whole of his body, and it seemed that he could survive only a few hours.

At that stage the situation was reviewed and it became obvious that his condition must have been caused by cardiac distress, for his airway was reasonably clear, his respiratory excursion appeared adequate, and so far as could be estimated, his tidal air did not seem to be unduly diminished. The fact that his subcutaneous emphysema had increased so much over the last few hours might also indicate increase of mediastinal pressure, and signs of mediastinal emphysema had increased slightly—his heart sounds being by now absent. Aspiration of the mediastinum was attempted again—about five or six hours after the previous exploration—that time a large amount of air being obtained from the third and fourth left intercostal spaces particularly. It was difficult to estimate the quantity as it was bubbled off under water, but probably it was of the order of thirty or forty millilitres. It was gratifying to see an immediate improvement in colour and to find that the heart sounds had become audible. For the remainder of the night his colour was maintained by needling of the mediastinum when indicated, frequent washing out of the trachea and the continuous administration of oxygen; throughout the whole of that night and the next day his trachea was held open with the dilator in the hands of a resident medical officer or nurse. Next day, the third after admission, no further aspiration of air was necessary, any cyanosis that appeared being due to mechanical blockage. The child was almost comatose and for a short time lost his swallowing reflex, but his condition improved after Dr. Raymond Hennessy provided him with a satisfactory tube longer than those in general use and of the lobster-tailed type, and advised the avoidance of sedatives in order to allow earlier awareness of obstruction as evidenced by restlessness. For the next two days he improved. The tube came out once and was reinserted as he became distressed. After four and a half days from tracheotomy the tube was removed with very little disturbance and he settled down well enough to phonate a little and to cough on request. By next day he was breathing mostly through his nose and mouth, phonation had improved, but his chest still gave evidence of a considerable quantity of mucus in the bronchioles. Since then his condition had steadily improved. His temperature and pulse rate fell gradually over the first ten days and had remained normal since. His chest was clinically clear, though he still had a loose cough. Most of the subcutaneous emphysema had disappeared, and his tracheotomy wound had almost healed.

Dr. McNeill said that unfortunately the causal organism was not known; none had been seen in smears, and the results of cultures were negative. A penicillin-insensitive staphylococcus was suspected in view of the slow response of the condition to one gramme of penicillin, 30 grammes of sulphadiazine, and four and a half grammes of streptomycin. The interesting feature of the case was the development so late as the second day of such a severe degree of mediastinal emphysema, amenable to treatment even at such an advanced stage and probably resulting from inability to cope adequately with such a deeply situated trachea, the partial obstruction provided by the ill-fitting tube being presumably the cause of its development. It was a relief to find that despite his prolonged and severe cyanosis, the child's mental faculties seemed to be unimpaired.

DR. H. MCLORINAN congratulated Dr. McNeill on an excellent result. He said that surgical emphysema was not uncommon after tracheotomy, but he had never seen it develop to such a degre as in the case under discussion. Expulsive coughing was, no doubt, a primary factor. The obvious cause therefore was the fact that the trachea was not quite clear and coughing was necessary to expel foreign matter (mucus). and so air was expelled into the tissues of the neck and soon reached the mediastinum. Dr. McLorinan added that he was sure that needling of the mediastinum was a most effective therapeutic measure in those cases and no doubt was responsible for the ultimate recovery of Dr. McNeill's patient. Considering the differential diagnosis in acute inflammation of the larynx and trachea, he said that four main groups could be separated. (i) Laryngeal spasm associated with a mild upper respiratory tract infection, such as a common cold. Some children were especially inclined to spasm of the laryngeal muscles. If the spasm was alleviated, they recovered quickly. (ii) Laryngeal diphtheria, either primary or secondary. The presence of membrane established the diagnosis of diphtheria. (iii) Staphylococcal, streptococcal and pneumococcal infections. In Dr. McLorinan's experience, most

cases of so-called laryngo-tracheo-bronchitis were caused by staphylococci. In those cases the patient came to operation most quickly. Large amounts of thick, dry, tenacious mucus formed in the trachea and bronchi, causing sudden attacks of dyspnœa as in Dr. McNeill's patient. The onset was rapid. (iv) *Hæmophilus influenzæ* infections. Those caused supraglottic œdema with great prostration, bacteriæmia and sudden collapse.

Dr. McLorinan said that the treatment of laryngo-tracheo-bronchitis due to staphylococcal infections consisted in giving diphtheria antitoxin, penicillin and sulphonamides and placing the patient in a steam tent. If any suspicions of *Hæmophilus influenzæ* infection were held, specific antiserum and streptomycin were employed. It was not easy to decide on the indications for tracheotomy in those cases. Intubation was unsuitable in the presence of much mucopurulent secretion as the tube became frequently blocked. Jackson of Philadelphia had admonished them not to be afraid to perform the operation of tracheotomy too early. The best guides were perhaps stridor and retraction going on for two or three hours with the early signs of exhaustion, pallor, rapid pulse, restlessness and sweating. If cyanosis had appeared, the operation had to be performed too rapidly and the risks were increased. Post-operative management was most important. A system of continual irrigation of the trachea and upper bronchi had been adopted. The unsatisfactory conditions were dry ones. It was Jackson who first pointed out that bronchopneumonia was not a common complication of tracheotomy and that most cases were due to obstruction below the tube, caused by accumulation of secretion. All methods employed were aimed at keeping the trachea and bronchi as moist as possible. One or two millilitres of sodium bicarbonate solution were instilled every half hour and the patient was kept in a warm moist atmosphere. A nurse stood by continually, inserting a catheter at intervals down the tracheotomy tube and sucking up the mucus as it formed. If that was unsuccessful, the tracheotomy tube was removed and the opening into the trachea was almost deluged with sodium bicarbonate solution, after which a rubber catheter sucker was inserted as far down as possible. That treatment might be required two or three times daily for four or five days. It was extraordinary the amount of manipulation that the children could stand. Rigid suckers were unnecessary and might cause trauma. If the rubber catheter was not successful, a bronchoscopist was called in. Dr. McLorinan said that he was quite certain that that method of keeping the passageway as moist as possible was best and in his experience had saved many lives. It must be combined with chemotherapy, especially with penicillin and sulphonamide. The case discussed was a most instructive one. He thought that the relief of the mediastinal emphysema was an important factor in the child's recovery, and he had learnt a lot from Dr. McNeill's demonstration.

DR. RAYMOND HENNESSY said that he would confine his remarks to the operation of tracheotomy. It was one of the oldest operations in surgery. There were records of its having been practised before the Christian era. The original operation was truly tracheotomy, actually the temporary opening of the trachea. As the modern operation invariably entailed the insertion of a tube which remained in the trachea for some hours or days, a mild protest might be raised against the use of the word tracheotomy, the operation being more correctly designated tracheostomy. The insertion of a cannula after the trachea had been opened dated back to the sixteenth century. The next development about one hundred and sixty years before was the use of a curved tube. Subsequent refinements were the use of an inner tube and shield with restraining tapes. That would be in about 1750. The operation was not practised very extensively until Trousseau in 1830 wrote about the great benefits of the operation in diphtheria, and since then it had become a routine and established surgical procedure.

Alluding to details about the tracheotomy tube, Dr. Hennessy said that most tubes were made on the principle of a small arc of a large circle. That was for rapidity of insertion. Fuller's bivalve tube, which Dr. Hennessy handed around, was an example of that and also of a tube which required no pilot. Obviously a tube that could be inserted easily might be expelled easily. To some extent that might be counteracted by the use of metal wings on the tube through which a tape was threaded and tied around the neck. By far the best tracheotomy tube for anything more than temporary use was Durham's, which was introduced in 1868. It was truly the Rolls Royce of tracheotomy tubes. Dr. Hennessy illustrated Durham's tube. He said that it would be observed that it was shaped like the letter J, with a short vertical and a long horizontal segment. Another feature was that there was an adjustable shield which allowed the lumen of the short vertical segment to be brought into line with the lumen of the trachea. There was no pressure therefore on the posterior wall. It was almost impossible for the patient to cough out that tube. With it a pilot was absolutely necessary, and Durham had ingeniously solved the problem by using the lobster-tailed device. Dr. Hennessy said that it would be observed that the inner tube was of a similar construction. When a tracheotomy tube had been worn for years there was no doubt whatever that Durham's was by far the most satisfactory. Durham was a surgeon of Guy's Hospital. Tracheotomy tubes for permanent use should be made of sterling silver. Cheaper tubes used only for short periods were generally made of German silver, but as the tracheal secretions caused much galvanic action between the inner and outer tubes, the life of the tubes was comparatively short owing to corrosion. The average life of a Durham's tube was eighteen months to two years of continuous wear.

Dr. Hennessy alluded to the operation known as laryngotomy. That truly did not open the larynx, as the incision was made through the crico-thyreoid membrane. It was an operation known only to older practitioners. Dr. Hennessy handed around a laryngotomy tube and said that it would be observed that its lumen was oval, distinguishing it at once from the round tracheotomy tube. The operation of tracheotomy might be extremely difficult. Much depended on the circumstances under which it had to be performed. When the operation could be done deliberately and slowly, the opening in the trachea should be through the third, fourth or fifth rings—the further away from the cricoid cartilage the better, because that was the only complete ring in the trachea. Stenosis was very likely to follow if the cricoid cartilage was damaged or cut. About five millilitres of 2% cocaine solution should be injected by an ordinary "Record" syringe into the trachea just before it was opened. That avoided a lot of distressing coughing and allowed a transquil and painless insertion of the tracheotomy tube. If a tube was to be worn for some time it was wise to cut a demilune on each side of the tracheal incision. That made the tracheal opening circular, corresponding with the round tracheotomy tube, and was preferable to pushing a circular tube through a linear slit. It was always desirable to have a loose fit between the metal tube and the tracheal opening because granulation tissue quickly developed on the cut edges of the tracheal cartilage. That acted as a kind of washer or collar between the metal and the trachea and ensured a snug fit eventually. In order to avoid emphysema it was wise never to sew up the integuments. That also diminished the risk of wound and mediastinal infection. When the operation had to be performed as a desperate emergency, refinements of technique, of course, were impossible. The only thing that should be striven for was to keep the opening in the trachea as far away from the cricoid cartilage as was possible. The after-care was important, and frequent, perhaps hourly, removal and cleansing of the inner tube might be necessary. The outer tube usually required removal and cleansing every twenty-four hours at the most. The indications for tracheotomy were to provide an airway in laryngeal obstruction, but the benefits of the operation were not confined to that. The tracheostomy drained the trachea of much secretion, mucus and pus, and also permitted continuous or intermittent instrumental suction, the benefits of which were admirably illustrated in the present case.

DR. VERNON COLLINS congratulated Dr. McNeill and the nursing staff. Dr. McNeill had devoted two whole nights to the patient. Laryngeal obstruction of that kind was one of the most difficult medical emergencies met with in practice. In the Children's Hospital the diagnosis and management were usually a responsibility of the resident staff. In view of Dr. McLorinan's remarks, it was apparent that the burden could be lightened, as the traditional advice about performing tracheotomy did not hold today. The old fear was bronchopneumonia, but it was not that but mucus obstruction that was the trouble. With penicillin and sulphonamide, the risk in tracheotomy was small, and it should be carried out more readily and frequently than in the past. Concerning mediastinal emphysema, the method of production was not clear till recently. It was at first thought to be due to rupture of alveoli. In the *Journal of Pediatrics* in 1947, Forbes and Salem had reveiwed 120 cases of tracheotomy and found that air tracked down from the tracheotomy wound. X-ray examination before tracheotomy showed no emphysema which could be demonstrated after the operation. It was seen mostly in the group with acute laryngo-tracheo-bronchitis. Many deaths occurred in the severe cases and recovery followed in some after needling of the mediastinum and after relief of the pneumothorax. The authors indicated that if bronchoscopy was performed before tracheotomy, the incidence of mediastinal emphysema was small.

DR. ROBERT SOUTHBY said that he had two questions to ask. Was it true, as held by some, that if intubation or the bronchoscopic tube was used before the tracheotomy it made the operation technically easier? Dr. McLorinan had stressed the imortance of keeping the secretions moist. The other extreme of keeping the air cold had been recommended especially in America. That was said to prevent drying up of the secretions.

DR. MURRAY CLARKE said that, as the father of a child saved after being almost moribund from the condition under discussion, he would be eternally grateful to Dr. McLorinan and his staff and would like to make one or two comments. The ordinary practitioner could not realize the high standard of nursing demanded in such cases. Nursing indeed reached its pinnacle there for meticulous attention to detail. His second comment was based on his experience as superintendent and registrar. That type of case was very worrying because of the inexperience of the staff in intubation and tracheotomy. In all cases therefore the patient should be referred immediately on diagnosis to a specialized institution such as that at Fairfield. Dr. Clarke said that that was not meant as a criticism of the management of the particular case under discussion. He asked what was the mortality in those cases and whether it had been altered by sulphonamide and penicillin therapy.

DR. W. KEOGH said that the question was not so much one of keeping the secretions moist as of keeping them less sticky. He wondered whether other agents than weak alkaline solution might be discovered, perhaps with the action of enzymes to help with the task.

Dr. McLorinan said that he could not see how intubation could stop the onset of emphysema. However, it was customary to try intubation first and it was sometimes dramatically successful; but one nearly always went ahead and performed tracheotomy. Dr. McLorinan said that he had no answer to offer concerning the use of the bronchoscope as advocated by Dr. Southby. He did not think a blast of cold dry oxygen was the best measure. In answer to Dr. Clarke, he said that the mortality had dropped in an extraordinary manner with the exhibition of sulphonamide and penicillin therapy and it was the exception for the patients to die. Dr. Keogh's remarks about better dissolving solutions were stimulating. The secretions were sometimes like scales.

# Australasian Medical Publishing Company, Limited.

## ANNUAL MEETING.

THE annual meeting of the Australasian Medical Publishing Company, Limited, was held at The Printing House, Seamer Street, Glebe, New South Wales, on October 13, 1948, and adjourned to October 20, 1948, Dr. W. L. Calov in the chair.

### Directors' Report.

The report of the directors of the company was as follows.

The directors submit their report for the twelve months ended June 30, 1948, together with the balance sheet as at June 30, 1948, and the profit and loss account for the twelve months ended June 30, 1948.

It is with the deepest regret that we report the death in England on November 19, 1947, of Dr. Thomas Walter Lipscomb, third chairman of directors, to whose memory a plaque has been erected at The Printing House, and the death in Brisbane on May 4, 1948, of Dr. David Gifford Croll. The late Dr. Lipscomb had been a member and director of the company from 1927, and chairman of directors from 1929 until his death. The late Dr. Gifford Croll was a member and director of the company from 1929. The directors of the company have placed on record their appreciation of the many years of valuable and disinterested service they gave to the company and to THE MEDICAL JOURNAL OF AUSTRALIA.

Dr. W. F. Simmons, of Forest Road and Herbert Street, Bexley, has been appointed to the Board to fill the casual vacancy caused by the death of Dr. T. W. Lipscomb.

During the year contributions to THE MEDICAL JOURNAL OF AUSTRALIA covered a wide range of subjects, but unfortunately shortage of paper and production difficulties have restricted plans to improve and enlarge the journal.

The result of the year's production in the printing and publishing department may be regarded as satisfactory in view of the present industrial conditions.

Depreciation amounting to £750 was written off during the year, and an amount of £1083 was transferred to the reserve for taxation. The company's reserves are used in the business, and we consider the state of the company's affairs is satisfactory.

Provision has been made for the payment of debenture interest for the year ended June 30, 1948.

Dr. W. L. Calov and Dr. A. E. Lee retire from office by rotation in accordance with the Articles of Association (Article 39). They are eligible and present themselves for reelection.

H. S. NEWLAND,
October 13, 1948. Chairman.

### Election of Directors.

Dr. W. L. Calov and Dr. A. E. Lee were reelected to the Board of Directors.

# Post-Graduate Work.

## THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

### Course in Advanced Medicine.

THE Post-Graduate Committee in Medicine in the University of Sydney desires to announce that a course in advanced medicine suitable for M.R.A.C.P. candidates will be conducted for a period of fifteen weeks from January 3 to April 14, 1949, the fee for which will be £39 7s. 6d. The programme has been arranged to take place almost exclusively in the afternoons from approximately 2 p.m. to 5 p.m. on five days per week. Extra sessions may be arranged on certain Saturdays. The course will include:

1. Didactic lectures on the more obscure aspects of internal medicine, designed to supplement the students' reading. These will cover the various systems in turn.
2. Lectures and tutorials in electrocardiography.
3. Ward rounds and demonstrations of cases at the principal metropolitan hospitals approximately twice weekly.
4. Regular clinico-pathological conferences.
5. Demonstrations of the *fundus oculi*.
6. Lecture-demonstrations in physiology and biochemistry and discussions on applied physiology.
7. Lecture-demonstrations in pathology and hæmatology.
8. Demonstrations of the application of radiological methods of diagnosis to medical diseases.
9. Demonstration of psychiatric cases.
10. The exhibition of selected medical films.
11. Portions of the annual post-graduate course of interest to students in advanced medicine.

The supervisor of the course, Dr. Selwyn G. Nelson, will conduct tutorials on selected subjects, and students may discuss with him any problems arising in the course of their work. It is expected that students will devote a considerable time to general reading, both of text-books and of current medical literature. The object of this course is to provide assistance and guidance for the serious students of internal medicine. It is desirable that students should have had considerable clinical experience in hospital and/or in medical practice before considering themselves prepared to take examinations for higher medical degrees or diplomas.

Fees are payable in advance at enrolment date and applications to attend whole or portion of this course should be in the hands of the Course Secretary, the Post-Graduate Committee in Medicine, 131, Macquarie Street, Sydney, not later than December 17, 1948. Telephones: BW 7483-B 6980. Telegraphic and cable address: "Postgrad, Sydney."

A further course in advanced medicine will be held for fifteen weeks later in the year, the probable commencement date of which is June 6, 1949.

# Special Correspondence.

## LONDON LETTER.

FROM OUR SPECIAL CORRESPONDENT.

### "? The Shape of Things to Come."

THE National Health Service has been running three months and it is freely admitted that members of the medical and dental professions are doing their best to make it work. Very few complaints have been made on behalf of the general public. One member of Parliament brought forward a series of charges, but when asked by the British

Medical Association to supply details refused to do so, and even the Minister of Health has been complimentary and has expressed appreciation of the work done. The usual crop of stories has appeared, such as that of the lady who rang her doctor late one evening and, when he had motored out to her home, opened the door and explained that she was not ill, but "wanted to see how the new system worked". Another "patient", when asked what was the matter with her, said: "Nothing, but the surgery is the most comfortable place I know of to sit in while waiting for my bus." The smaller committees are finding their powers are less than they expected and that much has to be referred to higher authority with consequent delay. Doctors unanimously complain of much more work, and many are seeking for assistants in practices which in the past had been worked single-handed. This has a more serious side, for, as one man puts it: "I am less sorry for myself than for the patients really in need of treatment. Often they have to wait an hour or two while the 'something for nothing' type is being dealt with. Quite half of those seen at present have nothing the matter with them. Everything is wrong with thousands who were perfectly well until the service came into operation." Such men look forward to the winter months with grave anxiety. Dentists and ophthalmologists also complain on this score of overwork even more than the doctors. In one area the cost of spectacles was reported to be seven times more than had been allowed for or expected. A dentist complained bitterly that "everyone in the town thinks he or she has some dental trouble and comes to me about it". The Minister of Health has appealed to people to be more moderate in their demands and only to seek advice medical, surgical, ophthalmic or dental when there is a real need. How much his request will be respected remains to be seen, but misgivings are voiced by those competent to judge. No doubt some of the present troubles will settle themselves in time, but an increase in the number of patients, with consequent rushed work, is being accepted as certain by all concerned in working the scheme.

Two other problems that only time will solve are already giving rise to some anxiety: First—will the scheme give a decent living to the doctor and also remain solvent? Second—the question of secrecy on professional matters between doctor and patients. In the House of Lords the Chancellor stressed the need for "proper certification" if the National Health Service was to succeed. Is the doctor to be on the side of the Chancellor of the Exchequer or is his patient to be his first consideration? The answers to these two questions are of paramount importance to the profession.

### "We Took Sweet Counsel Together: and Walked . . . as Friends."

This is the season for blackberries and conferences. The General Assembly of the World Medical Association met at Geneva on September 5 to 7 and proceedings were less hectic than at Paris last year. A spirit of sweet reasonableness permeated the meeting with a resultant improvement in the amount and quality of the work done. Politics could not be kept out entirely. The intention had been to hold this year's meeting at Prague, with Dr. Stuchlik in the chair. Recent events in Czechoslovakia led to the disbanding of the local national medical association and so the venue was changed to Switzerland with Professor Marquis as President. Much useful work was done and the World Medical Association may now be regarded as established and well on its feet; a sign of this is the decision to publish an official journal. In addition to the routine business many friendships were formed which will be of use in the future; the more we know of one another's difficulties the more we can help one another. The Assembly did not favour the State as the sole employer of the doctor, and recent tendencies this way were viewed with alarm and apprehension. The Hippocratic oath was discussed, particularly as to its inapplicability in part to present-day medical opinion. Attempts to bring the original text more into line with current thought were not entirely successful, but the subject is to be followed up. The discussion attracted a certain amount of adverse comment in the lay Press. *The Times* was sceptical as to the need for, or value of, any such venture, and the *Manchester Guardian* ridiculed the proposal. The action taken by the World Medical Association is ably defended in a recent *British Medical Journal*. After pointing out that "most national groups would today feel disinclined to pay homage to Apollo", as is laid down in the oath, the leader writer contends that "in these days of shifting values a cogent case can be made for drawing up in short and simple terms an ethical code to which medical men and women in any part of the world could respond". And so the matter stands.

The wide appeal for health among industrial workers was shown by the attendance of over 800 delegates, drawn from 46 countries, at the Eighth International Congress on Industrial Medicine held in London on September 13 to 17. Most of these delegates were doctors, so it was fitting that Lord Moran, President of the Royal College of Physicians, and Lord Webb-Johnson, President of the Royal College of Surgeons, should preside at the opening and closing sessions respectively. Discussions ranged widely, from organization to the special hazards in certain occupations, for industrial medicine is almost as universal in its application as medicine itself and touches nearly every aspect of the workers' efficiency and health. Lord Moran spoke wisely on the training of industrial medical officers; the budding industrial medical officer was no different to any other would-be specialist and must have a sound grounding in general clinical medicine before concentrating on his special work. This contention was supported by Dr. J. H. Gowland in the course of his remarks on organization, and is well illustrated by a recently issued and admirable report on the health of post office workers. And so the conferences come to a close and the delegates depart. As to the blackberries, for those who were able to get the necessary sugar, they still remain in the form of jam.

### "Welcome the Coming . . . Guest."

The following announcement in a recent *British Medical Journal* gave great pleasure and satisfaction to Australian doctors who know the man concerned.

> The Royal College of Physicians has nominated Professor G. W. Pickering, Professor of Medicine in the University of London, at St. Mary's Hospital, as the Commonwealth Travelling Professor for 1949. He will visit Australia and New Zealand in the early part of that year.

Professor Pickering is perhaps best known in connexion with his work on the circulation in general, and the renal circulation in particular, from both the clinical and physiological aspects. As the medical consultant at Harefield Hospital, in World War II, he had in his care such of our servicemen as were admitted to that hospital and was well liked.

### "Grave and Gay."

*Punch* supplies the following:

> For Your Shopping List.
>
> *"Lowered incidence of sensitization with sulphonamide combinations."*

(NOTE.—The words in quotation marks form the title of a paper in a journal most medical men do, and all should, read.)

## Correspondence.

### SINUSITIS AND SHORT-WAVE THERAPY.

SIR: Before dealing with Dr. Ernest Culpin's defence of the surgical approach to sinusitis in your journal of the 23rd instant, I should like to reply to his question put in the following form:

> I would like to ask Dr. Wilkie Smith to give his description of sinusitis and its origin and the rationale of treatment by short-wave therapy of the various nasal accessory sinuses. I would like to know how the short wave traverses or passes around the large air spaces present in the sinuses.

The question of a definition of sinusitis is loaded and would not be asked if it were easy to answer, but I see no reason to depart from the description in modern text-books which are available to Dr. Culpin. As to its origin, I believe the allergic factor is the initial and predominant cause in most cases of sinusitis. The sequence of events is probably traumatism of the sinusal cell by an endogenous blood-borne allergen, with cellular congestion, the discharge of histamine and functional disturbance of the cilia. The cell in this condition is vulnerable to trauma from the elements, and I believe that changes in humidity and cold air act as allies to the allergen in slowing the cilia. With static inactivity of the cilia the way is now prepared for invasion of the sinusal cell, and this is accomplished first by the common head cold virus, which prepares the way for one greater, in this case usually the streptococcus or staphylococcus. By self-replication, its greatest offensive weapon, and by the production of chemical enzymes, the virus which cannot live long outside the cell penetrates the cell by chemical abrasion of its membrane, and once this portal of entry is made the pyogenic

organisms can invade and complete the picture of suppurative sinusitis. I believe traumatism of the cell by an internal allergen and the discharge of histamine fits in with the reaction of inflammation, and that this condition could be designated an allergic sinusitis. As to what constitutes an allergen there is some doubt. According to Beadle's hypothesis, recently elaborated by Professor Burnet, an allergen can be regarded as one of mistaken identity as in the case of an antibody mistaking the identity of a proteinase for the one for which it was adapted. A simple illustration of this would be an antibody adapted to deal with or to digest the enzyme of meat, mistakes the identity of say; a lobster enzyme, attaches itself to it, fails to digest it and the resultant combination is an allergen. However, I must confess in treatment that I am more concerned with fat or its derivatives, possibly cholesterol as the active allergen. I believe ultimately it will be shown that Beadle's work on the gene of the cell nucleus will show a striking relation to the allergic manifestations with which we are dealing. Just as has been pointed out by Burnet, a certain type of idiocy can be ascribed to the absence of a gene in the nucleus, so I think in the allergic subject, particularly the asthmatic so prone to sinusitis, it will be shown that a gene is absent or dwarfed. This gene will be concerned mainly with lymphogenic activity. Space limits further discussion on this problem as also Dr. Culpin's request for the rationale of treatment of the nasal accessory sinuses. If he wants to know something of the condenser field and of its action on dielectrics and the rate of conduction through skin, subcutaneous tissue, fat, bone *et cetera* in the human body, and of its action upon steel, plastics and furniture in which it is now used for industrial purposes, he should consult books and papers on the subject to which I shall gladly refer him. Dr. Culpin knows the rationale of the therapeutic application of heat as well as I do, but the use of short-wave therapy in treatment of the human body is not just a matter of heat production or temperature rise. If this were so, why should a septic nail base respond to treatment by short-wave therapy in two days, in which the temperature rise is scarcely above body temperature, and fail to respond to hot foments or the immersion of the finger in almost boiling water? I believe one of the destructive agencies of short waves is the disturbance the oscillating wave causes to the reproductive cycle of the microorganism, which, as mentioned previously, is its chief weapon of offence. It is well known that the menstrual cycle in the human female can be influenced by the X ray and short wave.

Dr. Culpin says he knows "that sinus disease being a disease of the lining membrane, the disease does not recur in that particular sinus, such as the maxillary antrum, once the lining membrane is completely removed and efficient permanent drainage has been established". I ask what is the need of drainage if the membrane has been completely removed, for, according to Dr. Culpin, the disease should disappear with the removal of the membrane. Dr. Culpin writes with a facile pen as though this membrane can be removed as simply as stripping the skin from a banana. Later he says that "unless satisfactory permanent drainage is provided, true infection of the cavity can occur". How can the cavity be infected? I make this point because Dr. Culpin is going all round the most important question in dealing with chronic suppurative sinusitis, and that is involvement of the underlying bone. I have not succeeded in removing the lining membrane in a case of suppurative maxillary sinusitis, and I do not know any surgeon who has. A couple of years ago a patient of mine was in a hurry for a quick cure of maxillary sinusitis, and requested that a radical antrostomy be performed. This I refused, but at her request referred her to a senior colleague of undisputed reputation and skill who operated. After two months the radiological appearance of the antrum was the same as before operation and the symptoms worse, and twelve months later I received a note from America stating that she was in hospital recovering from a second antrostomy.

If the removal of this membrane is as easy as Dr. Culpin suggests, I challenge him or any surgeon to produce an aseptic antrum one month after a radical antrostomy has been performed on a suppurative maxillary sinusitis. The use of penicillin or any therapeutic agent will not be barred. The limit of one month will provide adequate time for the "cure" to be regarded as the result of operation.

Dr. Culpin makes great play of an episode in which he offered liberal odds to a young man if he could find six cases who had not improved following a radical antrostomy. He need only visit my surgery any day to find what he seeks and if necessary I shall gladly line up cases for him to interrogate. I do not fear the patients' reply. Finally, I should like to say that anyone who thinks he can treat sinus infection successfully by the application of short wave, by surgery or any other singular means is basing his hopes on false premises, for ultimately it will be shown that the cure is related to the cause.

Yours, etc.,

WILKIE SMITH.

Sydney,
October 26, 1948.

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SIR: Under the heading "Sinusitis and Short-Wave Therapy" in your issue of October 23, 1948, Dr. Culpin commences his letter by stating that he "cannot give a scientific discussion on the subject". I do not go so far, but only affirm that he certainly did not give any such discussion.

If we, as oto-rhino-laryngologists, cannot do better than group all diseases of the nasal accessory sinuses together as "nasal sinus disease", and then discuss it as a clinical entity, instead of under such headings as varieties of sinusitis, acute or chronic suppurative, varieties of fibrosis, post-inflammatory œdema, allergic œdema *et cetera*, the less said on the subject the better.

My reason, however, for making this letter as short as possible is other than this. I feel that the original article, which exhibited X-ray pictures of sinuses both before and many months after short-wave therapy as evidence of the efficacy of such treatment, when it is obvious that more numerous X rays could have been produced of parallel cases which had had no treatment at all, has already received more discussion than it deserved.

Yours, etc.,

A. B. K. WATKINS.

Commercial Bank Chambers,
Bolton Street,
Newcastle,
New South Wales.
October 25, 1948.

[This correspondence is now closed.—EDITOR.]

# Naval, Military and Air Force.

## APPOINTMENTS.

THE following appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 146, of October 15, 1948.

### AUSTRALIAN MILITARY FORCES.

### Interim Army.

*Australian Army Medical Corps: Medical.*

VX504193 Captain (Temporary Major) F. Grunseit relinquishes the temporary rank of Major, 1st July, 1948.

The date of transfer to the Reserve of Officers of SX700021 Captain P. G. Jay, which appeared in Executive Minute No. 39, of 1948, promulgated in *Commonwealth Gazette*, No. 49, of 1948, is amended to read "21st January, 1948".

SX34534 Captain R. G. McEwin is transferred to the Reserve of Officers (Australian Army Medical Corps) (4th Military District), 30th July, 1948.

130*th Australian General Hospital: To be Temporary Majors, 8th July*, 1948.—Captains VX700028 I. A. McDonald, NX506351 W. R. Vautin and SX700019 G. F. Cheeseman.

### Active Citizen Military Forces.

*Northern Command: Second Division.*

11*th Field Ambulance.*—1/39001 Lieutenant-Colonel C. F. Marks from command 7th Field Ambulance is appointed to command, 28th June, 1948.

*Eastern Command: Fixed Establishments.*

*Australian Army Medical Corps (Scientific).*—2/158684 Captain G. A. J. Pasfield is appointed from the Reserve of Officers, 1st May, 1948.

*Southern Command: Fourth Military District.*

*Australian Army Medical Corps (Medical).*—4/35214 Lieutenant-Colonel (Honorary Colonel) J. M. Dwyer, E.D., is appointed from the Reserve of Officers, 1st April, 1948, and is appointed Deputy Director of Medical Services, Headquarters, 4th Military District, 8th May, 1948 (in lieu of the notification respecting this officer which appeared in Executive Minute No. 93 of 1948, promulgated in *Commonwealth Gazette*, No. 116, of 1948).

4/31922 Captain G. C. Thornton is appointed from the Reserve of Officers, 1st May, 1948.

*Western Command: Fifth Military District.*

*7th/13th Field Ambulance.*—5/26391 Lieutenant-Colonel R. R. Anderson, M.C., from command 13th Field Ambulance is appointed to command, 28th June, 1949.

### Reserve Citizen Military Forces.

*Australian Army Medical Corps: First Military District.*

The notifications respecting the following officers which appeared in Executive Minute No. 188 of 1947, promulgated in *Commonwealth Gazette* No. 241 of 1947, are withdrawn: Majors C. F. Hecker, C. A. C. Leggett, M.B.E., and D. Watson, Honorary Major D. H. K. Lee, Captains C. R. Boyce, R. K. MacPherson, C. H. Mansfield, H. C. Murphy, T. R. Neville, C. W. Taylor and H. G. Wilson, and Honorary Captains R. V. Adamson, L. T. G. Geraghty, J. B. G. Gibson, N. F. George, F. Hatcher, B. C. Harvey, J. W. P. Henderson, P. F. Hyndes, A. M. Martell, H. P. Palethorpe, E. J. Ryan, S. M. Stephenson, C. G. Williams, N. V. Youngman and A. W. Chalmers.

*Australian Army Medical Corps: Fifth Military District.*

*To be Honorary Captain, 5th August,* 1948.—Noel Henry Maxwell Colyer.

ROYAL AUSTRALIAN AIR FORCE.

### Citizen Air Force.

*Medical Branch.*

The appointment of Temporary Wing Commander A. W. Raymond, O.B.E., M.C. (271218), is terminated on demobilization, 8th September, 1948.

### Reserve.

*Medical Branch.*

Ex-Wing Commander Arthur Wilmot Raymond, O.B.E., M.C. (271218), is appointed to a commission with the temporary rank of Wing Commander, 9th September, 1948. Frank Frederic Coffey (267843) is appointed to a commission with the temporary rank of Squadron Leader, 2nd March, 1948.

### Permanent Air Force.

*Medical Branch.*

George McLean (409563) is appointed to a short service commission with the rank of Flying Officer, 9th August, 1948, and he will take seniority as a Flying Officer from the date of his appointment.

Brian Stanley Woods (297502) is appointed to a short service commission with the rank of Flight Lieutenant, 20th September, 1948, and he will take seniority as a Flight Lieutenant from the date of his appointment.

## Australian Medical Board Proceedings.

### TASMANIA.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Act,* 1918, of Tasmania, as duly qualified medical practitioners.

Connolly, John Roger, M.B., B.S., 1947 (Univ. Sydney), Royal Hobart Hospital.
Watkins, George Bertram, M.B., B.S., 1947 (Univ. Sydney), Royal Hobart Hospital.
Oliver, John, M.B., B.S., 1947 (Univ. Sydney), Royal Hobart Hospital.
Correy, Joseph Frederick, 1947 (Univ. Sydney), Royal Hobart Hospital.
Walters, David John, M.B., B.S., 1947 (Univ. Sydney), Royal Hobart Hospital.
Sendak, Moses, M.R.C.S. (England), L.R.C.P. (London), 1926, M.B., B.S., 1927 (Univ. London), M.D., 1938 (Univ. London), D.P.H., R.C.S., 1937 (England), Port Cygnet.
Morey, Harry Francis, M.B., B.S., 1947 (Univ. Sydney), Ulverstone.

### QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of *The Medical Acts,* 1939 *to* 1946, of Queensland, as duly qualified medical practitioners.

Palmer, Calvin Henry, M.B., B.S., 1946 (Univ. Sydney), Hospitals Board, Maryborough.
Miller, Anthony Patrick, M.B., B.S., 1947 (Univ. Sydney), c.o. Hospitals Board, Bundaberg.
Barr, Stephen Grimwood, M.B., B.S., 1943 (Univ. Sydney), Commonwealth Health Laboratory, Toowoomba.
Deithe, Lyle George, M.B., B.S., 1947 (Univ. Sydney), Toowoomba Hospital, Toowoomba.
Bell, Malcolm, M.B., B.S., 1941 (Univ. Sydney), c.o. Dr. W. D. Rimmer, Walters Street, Lowood.
Murray-Jones, Judith, M.B., B.S., 1947 (Univ. Sydney), Cairns Hospital, Cairns.
Lake, Hilda Joy, M.B., B.S., 1947 (Univ. Sydney), Flat 2, Cragven, Hilderstone Street, Kangaroo Point, Brisbane.
Flynn, Robert Smollett, M.B., Ch.B., 1941 (Univ. St. Andrews), Rubislaw, Coventry Street, Hawthorne, Brisbane.
Spooner, Robert Dubois, M.B., B.S., 1947 (Univ. Sydney), c.o. Hospitals Board, Toowoomba.
Whaites, James Malcolm, M.B., Ch.B., 1944 (Univ. Edinburgh), D.O.M.S., R.C.P. and S., 1948 (England), Ballow Chambers, Wickham Terrace, Brisbane.

The following additional qualification has been registered.

Crosse, Walter Henry Burnham, Craigston, Wickham Terrace, Brisbane, D.L.O., 1948 (Univ. Sydney).

## Obituary.

### HENRY PATRICK BLANEY.

WE regret to announce the death of Dr. Henry Patrick Blaney, which occurred on October 3, 1948, at Howard, Queensland.

### OSBURN BRACEWELL GOYEN.

WE regret to announce the death of Dr. Osburn Bracewell Goyen, which occurred on September 27, 1948, at Beaudesert, Queensland.

### WILFRED ROBERT JOHN NICKSON.

WE regret to announce the death of Dr. Wilfred Robert John Nickson, which occurred on October 16, 1948, at Newcastle, New South Wales.

### JOHN ZIEGLER HUIE.

WE regret to announce the death of Dr. John Ziegler Huie, which occurred on October 23, 1948, at Rose Bay, New South Wales.

## Nominations and Elections.

THE undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Courtenay, Bruce Sturgess, M.B., B.S., 1947 (Univ. Sydney), Ryde District Soldiers' Memorial Hospital, Ryde.
Cronin, Kevin James, M.B., B.S., 1947 (Univ. Sydney), 3, Malvern Avenue, Chatswood.
Crowther, Geoffrey Earl, M.B., B.S., 1936 (Univ. Sydney), 9, Springfield Avenue, Darlinghurst.
Davies, George Bernard, M.B., B.S., 1947 (Univ. Sydney), c.o. Clifton Penny and J. R. Davies, "Templecourt", corner King and Elizabeth Streets, Sydney.
Davidson, George Madgwick, M.B., B.S., 1948 (Univ. Sydney), Sydney Hospital, Sydney.
Davidson, Doreen May, M.B., B.S., 1947 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Dent, John Arthur Sherbon, M.B., B.S., 1947 (Univ. Sydney), Western Suburbs Hospital, Croydon.
Duffy, Brian Thomas, M.B., B.S., 1946 (Univ. Sydney), Saint Joseph's Hospital, Auburn.

Dunlop, Donald Buzzard, M.B., B.S., 1946 (Univ. Sydney), Mater Misericordiæ Hospital, Waratah.

Dunlop, Roger John Massey, M.B., 1944 (Univ. Sydney), 10, Wentworth Street, Point Piper.

Dunn, David Brian, M.B., B.S., 1945 (Univ. Sydney), c.o. Mr. A. Booth, 771, Anzac Parade, Maroubra Junction.

Elton, Bruce Frederick, M.B., B.S., 1947 (Univ. Sydney), Balmain District Hospital, Balmain.

Failes, John Watson, M.B., B.S., 1945 (Univ. Sydney), Dalgarno Street, Coonabarabran.

Fewell, Dorothy Grace, M.B., B.S., 1947 (Univ. Sydney), 26, Rickard Road, South Hurstville.

Gough, Roy James, M.B., B.S., 1944 (Univ. Melbourne), Ivor Street, Henty.

Graham, Donald James, M.B., B.S., 1944 (Univ. Sydney), 2, Concord Road, Strathfield.

Grun, Ernest, M.B., B.S., 1947 (Univ. Sydney), 48, New South Head Road, Edgecliff.

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## Diary for the Month.

Nov. 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

Nov. 11.—Victorian Branch, B.M.A.: Organization Subcommittee.

Nov. 12.—Queensland Branch, B.M.A.: Council Meeting.

Nov. 15.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.

Nov. 16.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Nov. 17.—Western Australian Branch, B.M.A.: General Meeting.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

*New South Wales Branch* (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

*Victorian Branch* (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

*Queensland Branch* (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

*South Australian Branch* (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

*Western Australian Branch* (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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